A STUDY ON FACTORS INFLUENCING THE OUTCOME OF THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION

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Certificate

CERTIFICATE

This is to certify that this dissertation titled **"A STUDY ON FACTORS INFLUENCING THE OUTCOME OF THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION"** is submitted by **DR.PRATHEESH.P.P** to the **TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNA**I, in partial fulfillment of the requirement of the award of **M.D. DEGREE BRANCH I (GENERAL MEDICINE)** is a original research work carried out by him under our direct supervision and guidance.

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I solemnly declare that the dissertation titled **"A STUDY ON FACTORS INFLUENCING THE OUTCOME OF THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION"** was done by me from **March 2009 to October 2010** under the guidance and supervision of **Professor Dr. M RAVEENDRAN.M.D.**

This dissertation is submitted to the **TAMILNADU DR. M.G.R MEDICAL UNIVERSITY** towards the partial fulfillment of the requirement for the award of **M.D. DEGREE IN GENERAL MEDICINE (BRANCH I).**

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Contents

CONTENTS

Introduction

INTRODUCTION

Coronary heart disease (CHD) is a worldwide health epidemic. In the United States, for example, it is estimated that 13.7 million Americans have CHD, including more than 7.2 million individuals who already have had a myocardial infarction.[1,2] From the 1960's to the 1990's the CAD prevalence increased two fold (from 2% to 4%)in rural India and three fold (from 3.45 to 9.45%) in Urban India. The prevalence is even higher in South India (13% urban and 7% rural). In 1990, 25% deaths in India were attributable to cardiovascular disease compared to diarrheal disease ,12% due to respiratory infections and 5% due to tuberculosis[47]. In the group of persons older than 30 years of age, 213 per 100,000 individuals have CHD.[1] Although age-specific events related to CHD have fallen dramatically in the last few decades, the overall prevalence has risen as populations age and patients survive the initial coronary or cardiovascular event´. Worldwide 30 percent of all deaths can be attributed to cardiovascular disease of which more than half are caused by CAD.

Coronary Heart disease has been defined as impairment of heart function due to inadequate blood flow to heart compared to its needs caused by obstructive changes in the coronary circulation to the heart.

It is the cause of 25- 30% of deaths in most of the industrialized countries. In India also it is a major public health problem. It is aptly called by WHO as the modern epidemic. The increasing incidence of coronary heart disease may a reflection of increased longevity, adoption of high fat diet based on meats decreased exercise made possible by increasing affluence. It is not surprising to note that sir William Osler devoted only a few pages in his text book of

Medicine published in 1892 to the discussion of Acute myocardial infarction. It was the brilliant work of Herrick in 1912 who performed autopsy on acute myocardial infarction patients that put forward the new concept of thrombotic occlusion of coronary artery as the cause of downstream necrosis of the heart muscle. Definite proof for the above said concept came from angiographic studies performed during the early hours of the acute event. This promoted scientists to systematically test the thrombolytic strategies to treat acute myocardial infarction. Scientists have developed many effective thrombolytic drugs like streptokinase, recombinant tissue plasminogen activator (Alteplase), Reteplase, Urokinase, Tenecteplase etc.

Evidence for the use of thrombolytic therapy came from large multicentric studies. GISSI and ISIS -2 confirmed reduction in mortality with the early use of streptokinase. ISAM (intravenous streptokinase in acute

Myocardial Infarction study group) also stands as a proof of efficacy of thrombolytic drugs to reduce mortality.

Success rate of thrombolysis and thus the overall reduction in mortality is different among different agents used. The GUSTO-1 trial showed a 30 day mortality of 6.3 for accelerated t-PA verses 7.4% for streptokinase with intravenous heparin. In the GUSTO-1 trial in which alteplase was infused over 90 minutes there was a 14 % relative and a 1% absolute mortality reduction with alteplase compared with streptokinase at the cost of two extra strokes per 1000 patients randomized. In the GUSTO-III Trial reteplase was the equivalent to alteplase but there was less major bleeding. Reteplase and Teneceplase being given only once. The bolus agents do not reduce mortality but certainly more convenient simpler to use and help to reduce medication errors. Of all the agents alteplase, tenecteplase and reteplase are licenced[3] .

But because of the prohibitive cost of t-PA, reteplase, and tenecteplase ,streptokinase became the sheet anchor for the thrombolytic therapy in Coimbatore Medical College Hospital. Thrombolytic therapy has revolutionised the management of acute myocardial infarction. GUSTO angiographic substudy showed a success rate of 54% at 90 minutes using streptokinase and Heparin.

Thrombolytic therapy has been consistently proven to reduce the mortality and morbidity. Inspite of this it has been recognized that thrombolytic therapy has failed in significant population. There is lot of room for improvement. We need to identify the factors that are responsible for failure of thrombolysis.

In this background we decided to look into our own patients who receive streptokinase for acute myocardial Infarction, in the coronary care unit of Coimbatore Medical College Hospital.

Aim of the Study

AIM OF THE STUDY

1. To find out the overall success rate of thrombolysis in coronary care unit of Coimbatore medical college hospital.
2. To find out whether the following parameters influence the outcome of thrombolysis.
    1. Age
    2. Sex
    3. Pre-infarction angina
    4. Alcohol intake
    5. Smoking status
    6. Pre existing systemic hypertension
    7. Diabetes mellitus
    8. Type of Myocardial Infarction.
    9. Time interval between the onset of pain and the initiation of thrombolytic therapy.

Review of Literature

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

The origin of myocardial infarction - Already in ancient history it was noted that sudden pain in the chest could be a harbinger of death. The actual cause of death was not yet understood. First the circulation had to be described which was done by Harvey in the 17th century. Only at the beginning of the 20th century theories emerged on the Pathophysiology of myocardial infarction (MI), which was defined as necrosis of heart muscle tissue due to persisting ischemia. In 1910, Russian pathologists described five patients with acute MI of whom three showed coronary thrombosis at autopsy (Obraztsov,1910).

Subsequently, in 1912, Sir James Herrick wrote a publication on the syndrome of acute MI. He suggested that The clinical manifestations of coronary obstruction will evidently vary greatly depending on the size, location and number of vessels occluded. . Most of the observations hold good even after 90 years. So it was hypothesized for the first time that obstruction of the blood stream was the cause of subsequent necrosis and dysfunction of a part of the heart.[4] The introduction of cardiac catheterization settled this dispute. Using this technique, a thrombus was shown in patients with symptoms and ECG signs of MI (DeWood,1980).

This confirmed the view that acute thrombotic occlusion was the cause of MI. In addition, Falk and Davies showed that focal arterial lesions, in particular a fissured atherosclerotic plaque, were the origin of the thrombotic process (Falk,1983; Davies,1985). Adherence and aggregation of thrombi at the site of the culprit lesion preceded the development of fibrin (Davies,1979). Currently, the process of plaque rupture is more precisely understood (Richardson,1989; Chesebro,1991).[5]

PATHOLOGY

Almost all MIs result from coronary atherosclerosis, generally with superimposed coronary thrombosis. Before the fibrinolytic era, clinicians typically divided patients with MI into those suffering a Q-wave and those suffering a non-Q-wave infarct on the basis of evolution of the pattern on the ECG over several days. The term Q-wave infarction was frequently considered to be virtually synonymous with transmural infarction, whereas non-Q-wave infarctions were often referred to as subendocardial infarctions. Contemporary studies using cardiac magnetic resonance imaging indicate that the development of a Q-wave on the ECG is determined more by the size of the infarct than the depth of mural involvement.[6]

The hallmark of atherosclerotic coronary artery disease is the fibrous plaque.[7] Plaque disruption exposes substances that promote platelet activation and aggregation, thrombin generation, and ultimately thrombus

formation.[8,9] The resultant thrombus interrupts blood flow and leads to an imbalance between oxygen supply and demand and, if this imbalance is severe and persistent, leads to myocardial necrosis. The atherosclerotic plaques of patients who died of STEMI are composed primarily of fibrous tissue of varying density and cellularity with superimposed thrombus. Calcium, lipid-laden foam cells, and extracellular lipid each constitute 5 to 10 percent of the remaining area. A white thrombus is composed of platelets, fibrin, or both, and a red thrombus is composed of erythrocytes, fibrin, platelets, and leukocytes.

PLAQUE FISSURING AND DISRUPTION

Atherosclerotic plaques considered prone to disruption over express metalloproteinase enzymes such as collagenase, gelatinase, and stromelysin that degrade components of the protective extracellular matrix.[9] Activated macrophages and mast cells abundant at the site of atheromatous erosions and plaque disruption in patients who died of STEMI can elaborate these proteinases.[10] A number of key physiological variables such as systolic blood pressure, heart rate, blood viscosity, endogenous tissue plasminogen activator(t-PA) activity, plasminogen activator inhibitor-1 (PAI-1) levels, plasma cortisol levels, and plasma epinephrine levels exhibit circadian and seasonal variations and increase at times of stress.

ACUTE CORONARY SYNDROMES

When plaque disruption occurs, a sufficient quantity of thrombogenic substances is exposed, and the coronary artery lumen may become obstructed by a combination of platelet aggregates, fibrin, and red blood cells that may produce an extensive thrombus filling a large segment of the infarct-related artery. An adequate collateral network that prevents necrosis from occurring can result in clinically silent episodes of coronary occlusion. Disruption of plaques is now considered to underlie most acute coronary syndromes (ACS)[11] Characteristically, such completely occlusive thrombi lead to a large zone of necrosis involving the full or nearly full thickness of the ventricular wall in the myocardial bed subtended by the affected coronary artery and typically produce ST elevation on the ECG [2,3]. Infarction alters the sequence of depolarization ultimately reflected as changes in the QRS.[12] The most characteristic change in the QRS that develops in the majority of patients initially presenting with ST elevation is the evolution of Q waves in the leads overlying the infarct zone—leading to the term *Q*-wave infarction.[13] In the minority of patients presenting with ST elevation, no Q waves develop, but other abnormalities of the QRS complex are frequently seen, such as diminution in R wave height and notching or splintering of the QRS. Patients presenting without ST elevation are initially diagnosed as suffering either from unstable angina or NSTEMI .The ACS spectrum

concept, organized around a common pathophysiological substrate, furnishes a useful framework for developing therapeutic strategies.[14]ACS patients presenting without ST-segment elevation are not candidates for pharmacological reperfusion but should receive anti ischemic therapy, followed by PCI. All patients with ACS should receive antithrombin therapy and antiplatelet therapy regardless of the presence or absence of ST-segment elevation. Thus the 12-lead ECG remains at the center of the decision pathway for management of patients with ACS to distinguish between presentations with ST elevation and without ST elevation.[15,14]

THROMBUS FORMATION

Thrombus formation at the site of plaque disruption is the fundamental pathophysiological mechanism of unstable angina and acute myocardial infarction.

ROLE OF PLATELETS

This may be reviewed in three headings

- Platelet adhesion
- Activation with granular release
- Platelet aggregation

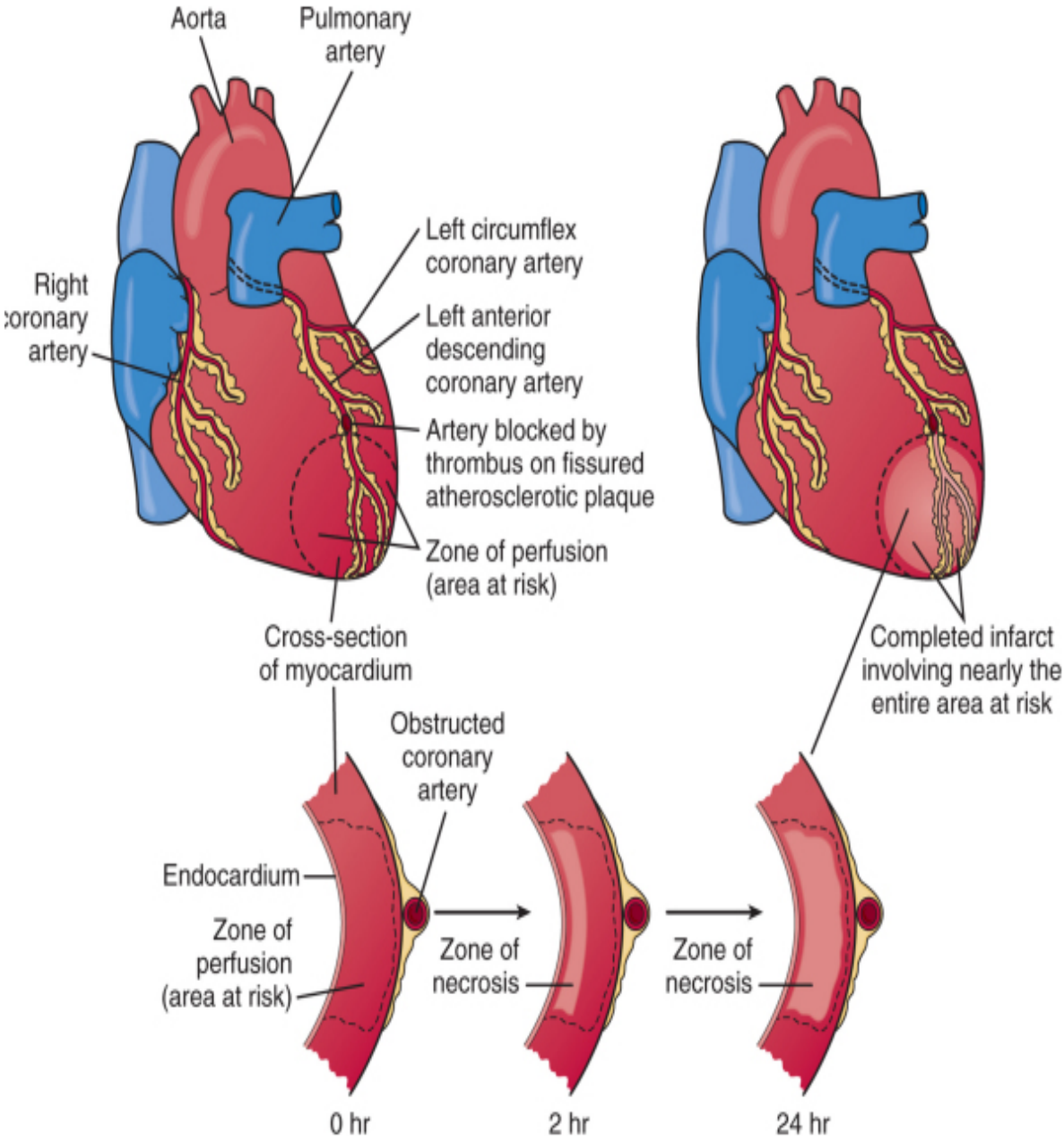


Fig 1 -Necrosis begins in a small zone of the myocardium beneath the endocardial surface in the center of the ischemic zone. This entire region of myocardium (dashed outline) depends on the occluded vessel for perfusion and is the area at risk. A narrow zone of myocardium immediately beneath the endocardium is spared from necrosis because it can be oxygenated by diffusion from the ventricle.

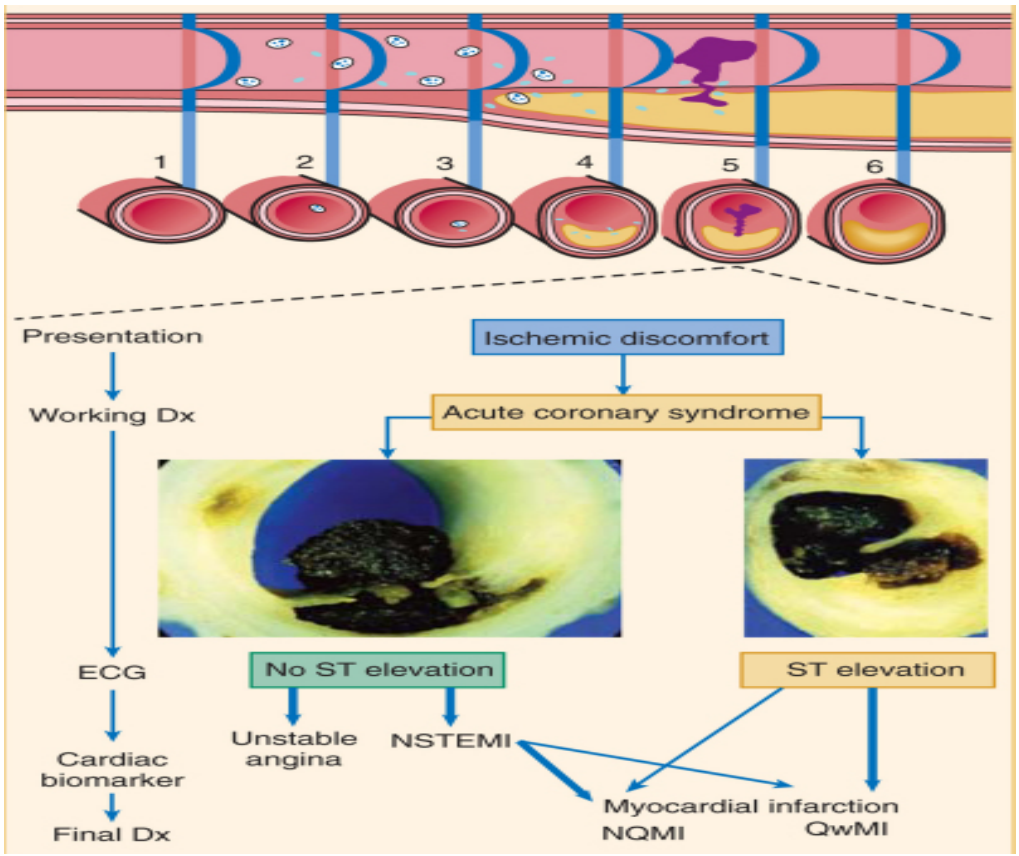


FIG 2 : Acute coronary syndromes. The longitudinal section of an artery depicts the "timeline" of atherogenesis from (1) a normal artery, to (2) lesion initiation and accumulation of extracellular lipid in the intima, to (3) the evolution to the fibrofatty stage, to (4) lesion progression with procoagulant expression and weakening of the fibrous cap. An acute coronary syndrome develops when the vulnerable or high-risk plaque undergoes disruption of the fibrous cap (5); disruption of the plaque is the stimulus for thrombogenesis. Thrombus resorption may be followed by collagen accumulation and smooth muscle cell growth (6). Following disruption of a vulnerable or high-risk plaque, patients experience ischemic discomfort resulting from a reduction of flow through the affected epicardial coronary artery. The flow reduction may be caused by a completely occlusive thrombus (**bottom half, right side**) or subtotally occlusive thrombus (**bottom half, left side**).

PLATELET ADHESION

Platelets adhere to the subendothelial collagen immediately. Glycoprotein 1b on the platelet membrane links with the von willebrand factor (VWF) in the subendothelial collagen. The membrane receptor complex Glycoprotein II b/IIIa bind a number of relevant protein including VWF , fibrinogen and fibronectin.

PLATELET ACTIVATION AND AGGREGATION

Activated platelets release a number of substances like serotonin, ADP, PDGF(Platelet derived growth factor) ,Thrombospondin, VWF etc. PDGF plays a role in the proliferation and migration of smooth muscle cells after vessel damage .Released ADP binds to the specific receptors that change the conformation of Gp II b/IIIa complex so that it binds vWf, fibrinogen, fibrinonectin thus linking adjacent platelet into the haemostatic plug.[16, 17, 18]

SYSTEMIC FACTORS FAVOURING THROMBOGENESIS

1.Circulating catecholamines increases the platelet aggregability and thrombi formation. Smoking and emotional factors may be operating by increasing the catecholamine levels in blood. 2. Elevated level of homocysteine :- This is toxic to endothelium and it decreases the capacity of endothelium to make nitric oxide and induces endothelium dysfunction. 3.Diabetes mellitus :- Apart from accelerated atherosclerosis platelet activity

and coagulation are increased in diabetics suggesting that it is a prothrombotic state.PAI –I levels are also found to be higher in diabetics . 4.Plasminogen Activator Inhibitor (PAI-I) :- High levels are associated with increased risk of Acute coronary syndromes. 5. Elevated Apolipoprotein (a) may serve as a competitive inhibitor of plasminogen and cause a prothrombotic stage. 6. Elevated fibrinogen and Factor VII :- It is another risk factor for thrombosis. Interestingly both are found to be elevated in advanced age, obesity, hyperlipidemia, diabetes, smoking and emotional stress. [19,21]

FIBRINOLYSIS

Fibrinolysis starts at the same time of thrombogenesis because elements of the fibrinolytic system are incorporated into the fibrin thrombus as it forms.

COMPONENTS OF FIBRINOLYTIC SYSTEM

1.PLASMINOGEN AND PLASMIN

Plasminogen is a single chain glycoprotein sythesised primarily by liver. This is the precursor of the chief proteolytic enzyme plasmin. This conversion is facilitated by the binding of the plasminogen to fibrin (thrombus). Plasmin is capable of proteolyzing not only fibrin but also other proteins like fibrinogen ,coagulation factors V,VIII and extracellular matrix protein.

2.PLASMINOGEN ACTIVATORS

Intrinsic activators of plasminogen are Kallikerin and Factor XIIa which are direct activators. Extrinsic activators are tissue type plasminogen activator (t-PA), High molecular weight two chain urokinase and Low molecular weight two chain Urokinase .EXOGENOUS ACTIVATORS :- These are used therapeutically in Acute Myocardial Infarction.Streptokinase , APSAC and staphylokinase belong to this category.

TISSUE TYPE PLASMINOGEN ACTIVATOR

(t-PA) is synthesized predominantely by vascular endothelial cells.It is a serine protease. In the absence of fibrin t-PA has little activity ,therefore t-PA mediated activation of plasminogen in the plasma is minimal. Both single and two chain form of t-PA have proteolytic activity that is enhanced several hundred fold in the presence of fibrin . Free plasmin in the plasma is rapidly neutralized by cx2-plasmin inhibitor where as fibrin bound plasmin in protected from (x2 plasmin inhibitor).[19,21,22]

UROKINASE TYPE PLASMIN ACTIVATORS

Urokinase is aserine protease that is synthesized in the kidney as well as in endothelial cells and initially released as a single chain Urokinase (scu-PA). Limited proteolysis by plasmin converts scu-PA to high molecular weight two chain urokinase (HMWtc UK). Like t-PA , HMW tc UK also

has relative fibrin selectivity but enhanced only 10 times by the presence of fibrin.

ENDOGENOUS INHIBITOR OF FIBRINOLYSIS

These inhibitors of plasminogen activators and plasmin belongs to serpin family. Thrombin induces PAI-I release from cultured human endothelial cells, so also endotoxin. During inflammatory states PAI –I levels are increased. There is diurnal variation in the circulating levels of PAI-I concentration which contribute to the clustering of Acute myocardial Infarction episodes during morning hours as well as resistance to thrombolytic therapy. PAI-2 is found in the placental tissue where it plays a role in hemostasis.

REGULATION OF FIBRINOLYSIS

Net activation of plasminogen is the result of a delicate balance among activators and inhibitors and protease receptor on the cell surface.Regulation and control of fibrinolysis occurs at several levels .Secretion of plasminogen activator inhibitor from endothelium,enhancement of plasminogen activation by fibrin and plasmin inhibition by alpha 2-antiplasmin inhibition .In addition certain cell types such as endothelial cells,monocytes and platelets have receptors for plasminogen activators which when occupied enhance plasminogen activation and localize plasmin activity to cell surface. By

modulating the expression of these cell surface receptors cellular regulation of fibrinolysis is possible.[20,21,22, 23]

ACUTE MYOCARDIAL INFARCTION

SYMPTOMS

Despite advances in the laboratory detection of STEMI, the patient's history remains crucial to establishing a diagnosis. The prodrome is usually characterized by chest discomfort, resembling classic angina pectoris, but it occurs at rest or with less activity than usual and can therefore be classified as unstable angina. A feeling of general malaise or frank exhaustion often accompanies other symptoms preceding STEMI.

NATURE OF THE PAIN

The pain of STEMI varies in intensity; in most patients, it is severe and in some instances intolerable. The pain is prolonged, usually lasting for more than 30 minutes and frequently for a number of hours. The discomfort is described as constricting, crushing, oppressing, or compressing; often the patient complains of a sensation of a heavy weight or a squeezing in the chest. The pain is usually retrosternal in location, spreading frequently to both sides of the anterior chest, with predilection for the left side. Often the pain radiates down the ulnar aspect of the left arm, producing a tingling sensation in the left wrist, hand, and fingers. . In some instances the pain of

STEMI may begin in the epigastrium and simulate a variety of abdominal disorders, a fact that often causes STEMI to be misdiagnosed as "indigestion." In some patients, particularly the elderly, diabetic patients, and heart transplantation recipients, STEMI manifests clinically not by chest pain but rather by symptoms of acute left ventricular failure and chest tightness or by marked weakness or frank syncope. Diaphoresis, nausea, and vomiting may accompany these symptoms

OTHER SYMPTOMS

Nausea and vomiting may occur, presumably because of activation of the vagal reflex or stimulation of left ventricular receptors as part of the Bezold-Jarisch reflex. These symptoms occur more commonly in patients with inferior STEMI than in those with anterior STEMI. [24]

GENERAL APPEARANCE

Patients suffering STEMI often appear anxious and in considerable distress. They often massage or clutch their chests and frequently describe their pain with a clenched fist held against the sternum (the Levine sign, named after Dr. Samuel A. Levine). Cough productive of frothy, pink, or blood-streaked sputum is common. Patients in cardiogenic shock often lie listlessly. Depending on the degree of cerebral perfusion, the patient in shock may converse normally or may evidence confusion and disorientation.

HEART RATE

The heart rate can vary from a marked bradycardia to a rapid regular or irregular tachycardia, depending on the underlying rhythm and the degree of left ventricular failure. Most commonly, the pulse is rapid and regular initially (sinus tachycardia at 100 to 110 beats/min), slowing as the patient's pain and anxiety are relieved; premature ventricular beats are common, occurring in more than 95 percent of patients evaluated within the first 4 hours after the onset of symptoms.

BLOOD PRESSURE

The majority of patients with uncomplicated STEMI are normotensive, although the reduced stroke volume accompanying the tachycardia can cause declines in systolic and pulse pressures and elevation of diastolic pressure. Among previously normotensive patients, a hypertensive response is occasionally seen during the first few hours, with the arterial pressure exceeding 160/90 mm Hg, presumably as a consequence of adrenergic discharge secondary to pain, anxiety, and agitation. Patients in cardiogenic shock by definition have systolic pressures below 90 mmHg and evidence of end-organ hypoperfusion. However, hypotension alone does not necessarily signify cardiogenic shock because some patients with inferior infarction with Bezold-Jarisch reflex activation may also transiently have systolic blood pressure below 90 mmHg.[25]

CAROTID PULSE

Palpation of the carotid arterial pulse provides a clue to the left ventricular stroke volume; a small pulse suggests a reduced stroke volume, whereas a sharp,brief upstroke is often observed in patients with mitral regurgitation or ruptured ventricular septum with a left-to-right shunt. Pulsus- alternans reflects severe left ventricular dysfunction.

THE CHEST

Moist rales are audible in patients who develop left ventricular failure and/or a reduction of left ventricular compliance with STEMI. Diffuse wheezing can present in patients with severe left ventricular failure. Cough with hemoptysis, suggesting pulmonary embolism with infarction, can also occur.

In 1967 Killip proposed a prognostic classification scheme on the basis of the presence and severity of rales detected in patients presenting with STEMI.[26]

Class I - patients are free of rales and a third heart sound.

Class II- patients have rales but only to a mild to moderate degree (<50 percent of lung fields) and may or may not have an S_3.

Patients in class III have rales in more than half of each lung field and frequently have pulmonary edema.

Class IV - patients are in cardiogenic shock. .[26,17]

CARDIAC EXAMINATION

Despite severe symptoms and extensive myocardial damage, the findings on examination of the heart may be quite unremarkable in patients with STEMI.

PALPATION

Palpation of the precordium may yield normal findings, but in patients with transmural STEMI, it more commonly reveals a presystolic pulsation, synchronous with an audible fourth heart sound, reflecting a vigorous left atrial contraction filling a ventricle with reduced compliance.

AUSCULTATION

HEART SOUNDS

The heart sounds, particularly the first sound, are frequently muffled and occasionally inaudible immediately after the infarct, and their intensity increases during convalescence.Patients with marked ventricular dysfunction and/or left bundle branch block may have paradoxical splitting of the second heart sound. A fourth heart sound is almost universally present in patients in

sinus rhythm with STEMI A third heart sound in patients with STEMI usually reflects severe left ventricular dysfunction with elevated ventricular filling pressure.

MURMURS

Systolic murmurs, transient or persistent, are commonly audible in patients with STEMI and generally result from mitral regurgitation secondary to dysfunction of the mitral valve apparatus (papillary muscle dysfunction, left ventricular dilation). A new, prominent, apical holosystolic murmur, accompanied by a thrill, may represent rupture of a head of a papillary muscle. The findings in cases of rupture of the interventricular septum are similar, although the murmur and thrill are usually most prominent along the left sternal border and may be audible at the right sternal border as well. The systolic murmur of tricuspid regurgitation (caused by right ventricular failure because of pulmonaryhypertension and/or right ventricular infarction or by infarction of a right ventricular papillary muscle) is also heard along the left sternal border.

FRICTION RUBS

Pericardial friction rubs may be heard in patients with STEMI, especially those sustaining large transmural infarctions.[28] Delayed onset of the rub and the associated discomfort of pericarditis (as late as 3 months

postinfarction) are characteristic of the now rare post myocardial infarction (Dressler) syndrome.

NEW DIAGNOSTIC CRITERIA FOR MYOCARDIAL INFARCTION

Criteria for acute, evolving or recent MI :- Either one of the following criteria satisfies the diagnosis for an acute, evolving or recent MI:

1) Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:

    a. ischemic symptoms;

    b. development of pathologic Q waves on the ECG;

    c. ECG changes indicative of ischemia (ST segment elevation or depression); or

    d. Coronary artery intervention (e.g., coronary angioplasty).

2) Pathologic findings of an acute MI.

Criteria for established MI:- Any one of the following criteria satisfies the diagnosis for established MI:

    1) Development of new pathologic Q waves on serial ECGs. The patient may or may not remember previous symptoms.

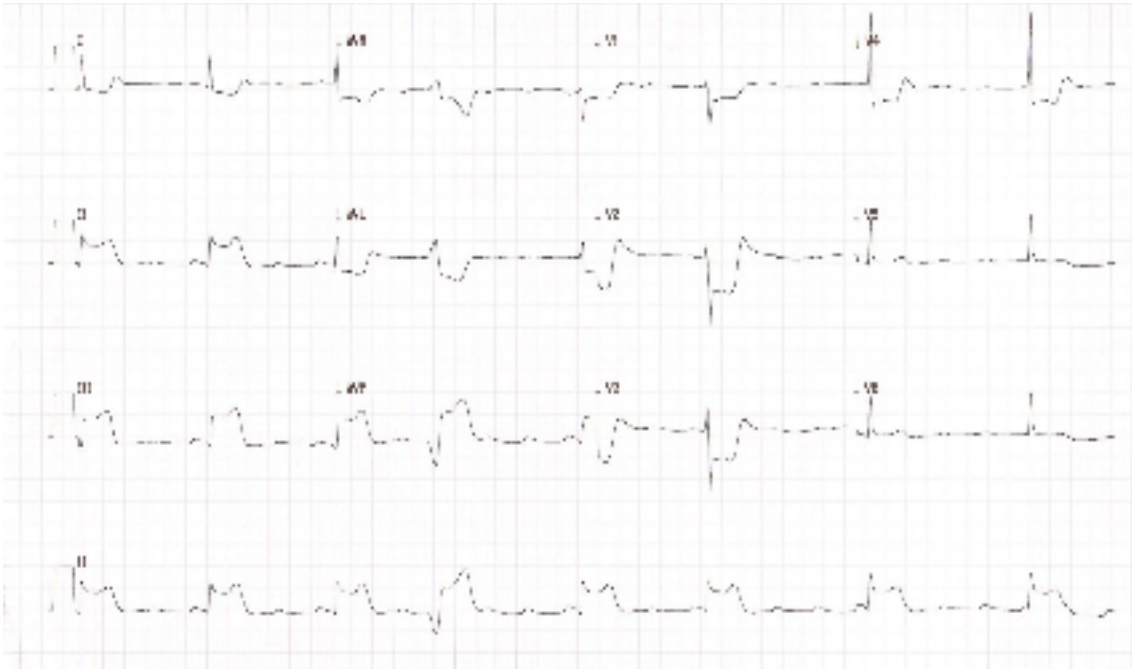
Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarct developed.

2) Pathologic findings of a healed or healing MI.[29,30,31]

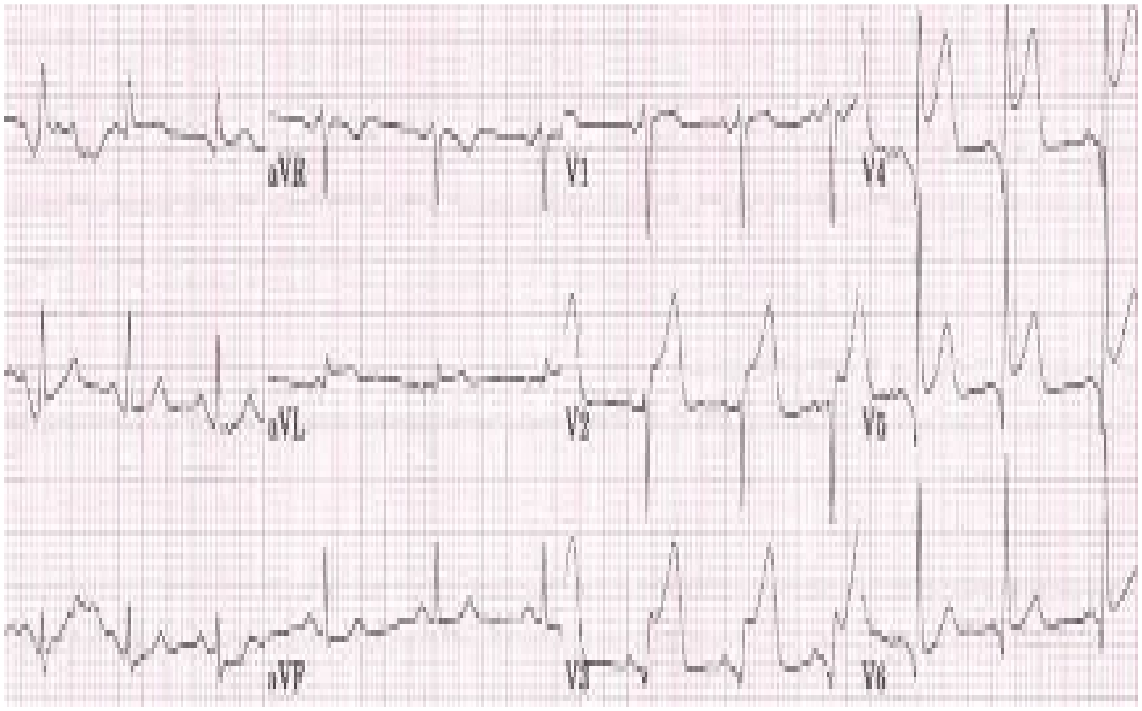
ELECTROCARDIOGRAPHIC CRITERIA

Electrocardiographic criteria for diagnosing acute myocardial infarction are the presence in the setting of chest pain of any one of the following,

1. New or presumably new Q waves (atleast 30ms wide and 0.20mV deep) in at least two leads in any of the following groups (a)lead II,III,avF(b)Leads V1-V6 (6)leads I and avL.
2. New or presumably new onset ST- elevation or depression >0.10mV measured 0.02 Sec after J point in two contiguous leads of the above mentioned lead combination.
3. New or presumably new complete LBBB



ECG Showing inferior wall myocardial infarction



ECG Showing anterior wall myocardial infarction

ELECTROCARDIOGRAPHIC ESTIMATE OF INFARCT SIZE

In general there is a direct relationship beween the number of leads showing st elevation and mortality.ST elevation in eight or nine lead is associated with a mortality of three to four times that of patients manifesting ST segment elevating in only two or three leads.

DIAGNOSIS OF RIGHT VENTRICULAR MI

ST segment elevation in lead V4R is the single most powerful indicator of right ventricular involvement in inferior wall myocardial infarction.

Localization of Ischemia or Infarction - The electrocardiographic leads are more helpful in localizing regions of transmural than subendocardial ischemia. As examples, ST elevation and/or hyperacute T waves are seen in the following: (1) one or more of the precordial leads (V_1 through V_6) and in leads I and aVL with acute transmural anterior or anterolateral wall ischemia; (2) leads V_1 to V_3 with anteroseptal or apical[32] ischemia; (3) leads V_4 to V_6 with apical or lateral ischemia; (4) leads II, III, and aVF with inferior wall ischemia; and (5) right-sided precordial leads with right ventricular ischemia. Posterior wall infarction, which induces ST elevation in leads placed over the back of the heart such as leads V_7 to V_9,[33] can be induced by lesions in the right coronary artery or left circumflex artery.

These lesions can produce both inferior and posterolateral injury, which may be indirectly recognized by reciprocal ST depression in leads V_1 to V_3. Similar ST changes can also be the primary electrocardiographic manifestation of anterior subendocardial ischemia. Posterior inferior wall infarction with reciprocal changes can be differentiated from primary anterior wall ischemia by the presence of ST segment elevations in posterior leads. The ECG can also provide more specific information about the location of the occlusion within the coronary system (the culprit lesion).[34,35,36,37] require additional validation in test populations.

S. No	Categories	Anatomy of Occlusion	ECG Features
1.	Left main disease	Left coronary artery	ST ↑ in aVR, ST ↓ in l,ll, v4 - v6 Sum of ST changes ≥18 mm
2.	Proximal LAD	Proximal to first septal perforator	.ST↑in V1- V6 / fascicular / budle branch block ST↑in V1≥2.5mm .ST ↑in avR .Disappearance of preexisting Q waves in lateral leads
3.	Mid Left anterior descending	Distal to first septal perforator, proximal to large diagonal	ST↑ V1 –V6 , L1, aVL
4.	Distal LAD or diagional	Distal to large diagonal or diagonal it self	ST ↑ V1 – V4 ,or ST↑ in 1, AVL,V5 ,V6

5.	Moderate to large inferior	Proximal RCA or left circumflex	ST ↑ ll,lll,avF,and any of the following V1,V3R,V4R V5 - V6 ,R > S in V1 , V2
6.	Small inferior	Distal RCA or left circumflex branch occlusion	ST ↑ ll,lll, avF only

Enzymatic criteria for diagnosis of acute myocardial infarction

1. Serial increase and then decrease of plasma CK-MB with change of >25 % between two values.
2. CK-MB >10-13U/ L or >5% OF TOTAL CK activity.
3. Increase in CK-MB activity >50% between any two samples separated by at least 4 hours.
4. If only a single available CK-MB elevation > two fold.
5. 5.Beyond 72 hours an elevation of Troponin T or Troponin I or LDH-1>LDH-2

MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION

Immediately begin continuous cardiac monitoring for patients with suspected ischemic type of chest pain and obtain intravenous access

Treatment for the STEMI Patient

1.	Condition: continuous monitoring of cardiac status in ccu
2.	IV: NS on D_5W to keep vein open. Start a second IV if IV medication is being given. This may be saline lock.
3.	Vital signs: every 1.5 hr until stable, then every 4 hr and as needed. Notify physician if HR is <60 beats/min or > 100 beats/min, BP is <100 mm Hg systolic or >150 mm Hg systolic, respiratory rate is < 8 or > 22.
4.	Monitor: Continuous ECG monitoring for dysrhythmia and ST segment deviation
5.	Diet: NPO except for sips of water until stable. Then start 2 gm sodium/day, low saturated fat (<7% of total calories/day), low cholesterol (<200 mg/day) diet, such as total lifestyle change (TLC) diet
6.	Activity: Bedside commode and light activity when stable
7.	Oxygen: Continuous oximetry monitoring. Nasal cannula at 2 liters/min when stable for 6 hr, reassess for oxygen need (i.e., O_2 saturation of <90%) and consider discontinuing oxygen.
8.	Medications:
a.	Nitroglycerin (NTG) 1. Use sublingual NTG 0.4 mg every 5 min as needed for chest discomfort. 2. Intravenous NTG for CHF, hypertension, or persistent ischemia.

b.	Aspirin (ASA; acetylsalicylic acid) 1. If ASA not given in the emergency department (ED), chew nonenteric-coated ASA 162-325 mg. 2. If ASA has been given, start daily maintenance of 75-162 mg daily; may use enteric coated for gastrointestinal protection.
c.	Beta blocker If not given in the ED, assess for contraindication (i.e., bradycardia and hypotension); continue daily assessment to ascertain eligibility for beta blocker. If given in the ED, continue daily dose and optimize as dictated by heart rate and blood pressure.
d.	Angiotensin-converting enzyme (ACE) inhibitor 1. Start ACE inhibitor orally in patients with pulmonary congestion or LVEF <40 percent if the following are absent: hypotension (SBP <100 mm Hg or <30 mm Hg below baseline) or known contraindications to this class of medications.
e.	Angiotensin receptor blocker (ARB) 1. Start ARB orally in patients who are intolerant of ACE inhibitors and with either clinical or radiological signs of heart failure or LVEF <40 percent.
f.	Pain medications IV morphine sulfate 2-4 mg with increments of 2-8 mg IV at 5- to 15-min intervals as needed to control pain.
g.	Anxiolytics (based on a nursing assessment)
h.	Daily stool softener

GENERAL TREATMENT MEASURES

ASPIRIN

This agent is not only useful for the primary prevention of vascular events but is also effective across the entire spectrum of acute coronary syndromes and forms part of the initial management strategy for patients with suspected STEMI. The goal of aspirin treatment is to quickly block formation of thromboxane A_2 in platelets by cyclooxygenase inhibition. Because low doses (40 to 80 mg) take several days to achieve full antiplatelet effect, at least 162 to 325 mg should be administered acutely in the emergency department.[48] To achieve therapeutic blood levels rapidly, the patient should chew the tablet to promote buccal absorption rather than absorption through the gastric mucosa.

CONTROL OF CARDIAC PAIN

Analgesia is an important element of management of STEMI patients in the emergency department. Pain contributes to the heightened sympathetic activity that is particularly prominent during the early phase of STEMI. Control of cardiac pain is typically accomplished with a combination of nitrates, analgesics (e.g., morphine), oxygen, and beta-adrenoceptor receptor blockers .Morphine remains the drug of choice, except in patients with well-documented morphine hypersensitivity. 4 to 8 mg should be administered intravenously, and doses of 2 to 8 mg repeated at intervals of 5 to 15 minutes

until the pain is relieved or evident toxicity,hypotension, depression of respiration, or severe vomiting—precludes further administration of the drug.

NITRATES

By virtue of their ability to enhance coronary blood flow by coronary vasodilation and to decrease ventricular preload by increasing venous capacitance, sublingual nitrates are indicated for most patients with an acute coronary syndrome. At present, the only groups of patients with STEMI in whom sublingual nitroglycerin should not be given are those with inferior MI and suspected right ventricular infarction[49] or marked hypotension (systolic pressure <90 mm Hg), especially if accompanied by bradycardia. Once it is ascertained that hypotension is not present, a sublingual nitroglycerin tablet should be administered and the patient observed for improvement in symptoms or change in hemodynamics. If an initial dose is well tolerated and appears to be of benefit, further nitrates should be administered, with monitoring of the vital signs.

BETA BLOCKERS

These drugs relieve pain, reduce the need for analgesics in many patients, and reduce infarct size and life-threatening arrhythmias. Avoiding early intravenous blockade in patients presenting in Killip Class II or greater is important, however, because of the risk of precipitating cardiogenic shock.

[50,51] A popular and relatively safe protocol for the use of a beta blocker in this situation is as follows. (1) Patients with heart failure (rales >10 cm up from diaphragm), hypotension (blood pressure <90 mm Hg), bradycardia (heart rate <60 beats/min), or heart block (PR interval >0.24 sec) are first excluded. (2) Metoprolol is given in three 5-mg intravenous boluses. (3) Patients are observed for 2 to 5 minutes after each bolus, and if the heart rate falls below 60 beats/min or systolic blood pressure falls below 100 mm Hg, no further drug is given. (4) If hemodynamic stability continues 15 minutes after the last intravenous dose, the patient is begun on oral Metoprolol, 50 mg every 6 hours for 2 days, then switched to 100 mg twice daily. An infusion of an extremely short-acting beta blocker, Esmolol (50 to 250 mg/kg/min), may be useful in patients with relative contraindications to beta blockade in whom heart rate slowing is considered highly desirable.

OXYGEN

Hypoxemia can occur in patients with STEMI and usually results from ventilation-perfusion abnormalities that are sequelae of left ventricular failure .Treating all patients hospitalized with STEMI with oxygen for at least 24 to 48 hours is common practice on the basis of the empirical assumption of hypoxia and evidence that increased oxygen in the inspired air may protect ischemic myocardium. However, this practice may not be cost-effective. oxygen should be administered to patients with STEMI when

arterial hypoxemia is clinically evident or can be documented by measurement (e.g., SaO_2 <90 percent).[48] In these patients, serial arterial blood gas measurements can be employed to follow the efficacy of oxygen therapy. The delivery of 2 to 4 liters/min of 100 percent oxygen by mask or nasal prongs for 6 to 12 hours is satisfactory for most patients with mild hypoxemia.

LIMITATION OF INFARCT SIZE

In view of the prognostic importance of infarct size, the concept that modification of infarct size is possible has attracted a great deal of experimental and clinical attention.[52,53] Efforts to limit the size of the infarct have been divided among several different (sometimes overlapping) approaches: (1) early reperfusion, (2) reduction of myocardial energy demands, (3) manipulation of sources of energy production in the myocardium, and (4) prevention of reperfusion injury.

Assessment of Reperfusion Options for STEMI Patients

Step 1: Assess time and risk.

Time since onset of symptoms ,Risk of STEMI , Risk of fibrinolysis ,Time required for transport to a skilled PCI laboratory

Step 2: Determine fibrinolysis or invasive strategy is preferred.

If presentation is <3 hr and there is no delay to an invasive strateg y, there is no preference for either strategy.

Fibrinolysis is generally preferred if:

1. Early presentation (≤3 hr from symptom onset and delay to invasive strategy),
2. Invasive strategy is not an option - Catheterization laboratory occupied or not available, Vascular access difficulties, Lack of access to a skilled PCI laboratory
3. Delay to invasive strategy - Prolonged transport , Door-to-Balloon)–(Door-to-Needle) more than 1 hr, Medical contact-to-balloon or door-to-balloon more than 90 min

An invasive strategy is generally preferred if:

1. Skilled PCI lab is available with surgical backup ,
2. Skilled PCI lab is available, defined by - Medical contact-to-balloon or door-to-balloon less than 90 min, Door-to-balloon)–(door-to-needle) less than 1 hr , High risk from STEMI, Cardiogenic shock, Killip class ≥3, Contraindications to fibrinolysis including increased risk of bleeding and ICH, Late presentation, Symptom onset was more than 3 hr ago, Diagnosis of STEMI is in doubt

HISTORY OF THROMOLYSIS

Human blood has long been known to contain fibrinolytic activity. Well over 110 years ago Denys and Zimmerman observed that the fibrin of human blood obtained from wet cupping dissolved in 12 to 24 hrs. Dastre coined the term fibrinolysis.

The property of spontaneous thrombolysis was used by Yudin of Russia who used blood from fresh copses (who were previously healthy, but died of accidents) for transfusion.

In 1933 Tillet and Garner at the John Hopkin's medical school demonstrated that filtrates of both cultures of certain of hemolytic streptococcus contained a substances capable of inciting rapid fibrinolysis of human plasma clots.They named it streptococcal fibrinolysin.

Christensen renamed it streptokinase in 1945.He demonstrated that SK activates an inactive precursor of a proteolytic enzyme,later found to be plasminogen.

Streptokinase was clinically used first in 1947 by Tillet and Sol sherry in a young man who developed loculated bloody effusion in the left pleural cavity following pneumonectomy.The response was dramatic in that all the loculation were broken and a lysed coagulam was drained. In 1977 FDA

approved streptokinase and Urokinase for clinical use which opened the new clinical era of reperfusion therapy.[54,55,56]

THROMBOLYTIC DRUGS

NON FIBRIN SELECTIVE

STREPTOKINASE:-Streptokinase is produced by beta-hemolytic streptococci. Streptokinase by itself is not a plasminogen activator, but it binds with free circulating plasminogen (or with plasmin) to form a complex that can convert additional plasminogen to plasmin. Streptokinase activity is not enhanced in the presence of fibrin. Streptokinase is the least expensive fibrinolytic agent, but, unfortunately, it is antigenic and produces a high incidence of untoward reactions. This drawback limits the usefulness of streptokinase in the clinical setting. Although other fibrinolytic agents are more popular in developed nations like the United States, streptokinase continues to be widely used in developing nations. Studies with radioactive streptokinase indicate two disappearance rates: a "fast" half-life of approximately 18 minutes and a "slow" half-life of approximately 83 minutes.[57,58] Since it is produced from streptococcal bacteria, it often causes febrile reactions and other allergic problems. It can also cause hypotension that appears to be dose related. Streptokinase usually cannot be administered safely a second time within 6 months, because it is highly antigenic and results in high levels of antistreptococcal antibodies.[57,58,59]

Adverse effects :- Hypotension is the most common adverse effect which ranges from 10 – 40 % of SK administration.Allergic reactions reported included fever ,chills,urticaria,rash,flushing and muscle pain.Minor bleeding can occur especially from vascular puncture and access site.Manual compression for 30 mts or until bleeding stops is usually effective.Intracranial bleeding is the dreaded complication. Total stoke incidence in GISSI/international trial was 0.9%,in ISIS 3 trial it was 1%.[57,58]

MODE OF ADMINISTRATION

1.5million units of SK administrated over 1 hour is the standard regimen.More rapid administration can lead to hypotension and should be avoided.

Urokinase 2

Urokinase (Abbokinase, Kinlytic) [58 ,60] is the fibrinolytic agent most familiar to interventional radiologists and the one that has been used most often for peripheral intravascular thrombus and occluded catheters. Urokinase is a physiologic thrombolytic agent that is produced in renal parenchymal cells. Unlike streptokinase, urokinase directly cleaves plasminogen to produce plasmin. Allergic reactions are rare, and the agent can be administered repeatedly without antigenic problems

RELATIVELY FIBRIN SPECIFIC AGENTS : TISSUE TYPE PLASMINOGEN ACTIVATOR (t-PA)

Alteplase (tPA, Activase) was the first recombinant tissue-type plasminogen activator and is identical to native tissue plasminogen activator. It is the physiologic thrombolytic agent responsible for most of the body's natural efforts to prevent excessive thrombus propagation. Alteplase is fibrin specific with a plasma half-life of 4-6 minutes. It is the fibrinolytic agent most familiar to emergency departments.[40,41] Alteplase may be re-administered as necessary, as it is not antigenic and almost never is associated with any allergic manifestations. The accelerated infusion of alteplase (tPA) for acute MI is 15 mg IV bolus, followed by 0.75 mg/kg (up to 50 mg) IV over 30 minutes, then 0.5 mg/kg (up to 35 mg) IV over 60 minutes. The maximum total dose is 100 mg for patients weighing >67 kg. This is the most common alteplase infusion parameter used for acute myocardial infarction.

Reteplase

(r-PA, Retavase) is a second-generation recombinant tissue-type plasminogen activator that seems to work more rapidly and to have a lower bleeding risk than the first-generation agent alteplase.

Tenecteplase (TNKase)

TNKase was approved by the FDA as a fibrinolytic agent in 2000. This drug has a similar mechanism of action as alteplase (tPA). It is the latest thrombolytic agent approved for use in clinical practice. TNKase is currently indicated for the management of acute myocardial infarction (AMI). [42] TNKase has the advantage for a single bolus administration and decreased bleedingside effects due to high fibrin specificity. The ASSENT-2 trial evaluated the efficacy and safety of tenecteplase compared with alteplase in patients with AMI. Tenecteplase was found noninferior to alteplase in terms of 30-day mortality.[43] Follow-up study showed that mortality rates between the two active therapy groups remained similar after one year.[44]

PATENCY OF INFARCT RELATED ARTERY

Angiographic assessment :- TIMI grading is used to assess the angiographic patency

Grade of flow	Definition
0	Complete occlusion
1	Penetration without perfusion.Coronary bed distal to occlusion fails to opacify completely.
2	Partial perfusion .Full but slow opacification of coronary bed distal to occlusion.
3	Complete perfusion

CLINICAL DETECTION OF REPERFUSION

Sudden disappearance of chest pain is associated with successful thrombolysis.But this is difficult to assess in the CCU setup when most of the patients receive opioid analgesics.

ECG : A BETTER PREDICTOR OF PERFUSION AT MICROVASCULAR LEVEL

Recent studies have suggested that achievement of TIMI grade flow in infarct related artery is not itself indicative of successful myocardial reperfusin.[61,62] Myocardial contrast echocardiography has shown that even in the presence of normal epicedial flow after PTCA impaired myocardial perfusion at tissue level can occur and is associated with poor recovery of LV function. Resolution of ST-segment elevation on the surface ECG correlates closely with findings at contrast echocardiography.[63] Less than 5 0% resolution of ST- segment elevation in the worst lead and no accelerated idioventricular rhythm has sensitivity of 81 %, specificity of 88% positive predictive value of 87%,negative predictive value of 83% and overall accuracy of 85% in prdecting < TIMI 3 flow in infact related vessels. [64]

PROGNOSTIC SIGNIFICANCE OF ST RESOLUTION

James A de lemos et al. reported that 30 days mortality was 2.4% among patients who attain >70% ST resolution at 90 minutes where as it was 8.1% in those with <30% ST resolution. [65]

FACTORS INLUENZING THE SUCCESS OF THROMOLYSIS

1. **TIME INTRAVAL BETWEEN PAIN ONSET AND TO INITIATION OF THROMBOLYTIC THERAPY :** Thus is the most important variable affecting the success of thrombolysis. As the window boardens not only more and more myocardium gets necrosed but also thrombus gets organized and become more resistant to lysis.

2. **STRUCTURE OF THROMBI :** Thrombi rich in platelets are more resistant to lysis than fibrin rich thrombi.

3. **CIRCARDIAN RHYTHM :** A morning resistence to thrombolytic therapy was observed by Braunwald et al . Where as better success rate of thrombolysis was found by E Gold Hammer et al. When SK was administterd between 4:00pm – 8:00pm hours.

4. **PREINFARCTION ANGINA :** Patients with acute myocardial infarction who have intermittent infarct related pain or unstable angina in the seven days preceding the infarction have faster coronary artery perfusion and smaller infarsts after thrombolytic therapy than patients without preinfarction angina. (24) this may be an additional mechanism for the better prognosis in these patients ,the other proposed mechanism being ischemic preconditioning.

5. **SEX :** Eventhough mortality is high among woman who develop acute myocardial infarction,compared to men ,the rate of induction of coronary patency with thrombolytic drugs are coparable in woman.Mensturation is not a contraindication for thrombolytic therapy because menstrual bleeding is related more to sloughing of tissue than active bleeding.

6. **CONGESTIVE HEART FAILURE AND CARDIOGENIC SHOCK :** No significant reduction in mortality occurs when the killip class IV patients are treated with SK. This may be due to low rate of adequate recanalisation.

7. **ELDERLY PATIENT :** Risk of hemorrhagic complications are high in those aged above 75 years.

8. **REPERFUSION INJURY :** The process of reperfusion, although beneficial in terms of myocardial salvage, may come at a cost because of a process known as reperfusion injury. Several types of reperfusion injury have been observed in experimental animals. These consist of (1) lethal reperfusion injury—a term referring to reperfusion-induced death of cells that were still viable at the time of restoration of coronary blood flow; (2) vascular reperfusion injury—progressive damage to the microvasculature such that there is an expanding area of no reflow and loss of coronary vasodilatory reserve; (3) stunned

myocardium—salvaged myocytes display a prolonged period of contractile dysfunction following restoration of blood flow because of abnormalities of intracellular metabolism leading to reduced energy production; and (4) reperfusion arrhythmias—bursts of ventricular tachycardia and on occasion ventricular fibrillation that occur within seconds of reperfusion.[66,67] The available evidence suggests that vascular reperfusion injury, stunning, and reperfusion arrhythmias can all occur in patients with STEMI.

REPERFUSION ARRHYTHMIAS

Transient sinus bradycardia occurs in many patients with inferior infarcts at the time of acute reperfusion; it is most often accompanied by some degree of hypotension. This combination of hypotension and bradycardia with a sudden increase in coronary flow has been ascribed to the activation of the Bezold-Jarisch reflex.[48,68,69] Premature ventricular contractions, accelerated idioventricular rhythm, and nonsustained ventricular tachycardia are also seen commonly following successful reperfusion.

CATHETER-BASED REPERFUSION STRATEGIES

Reperfusion of the infarct artery can also be achieved by a catheter-based strategy. This approach has evolved from passage of a balloon catheter over a guidewire to now include potent antiplatelet therapy (intravenous

glycoprotein [GP] IIb/IIIa inhibitors, thienopyridines) and coronary stents.[48] When PCI is used in lieu of fibrinolytic therapy, it is referred to as direct or primary PCI. When fibrinolysis has failed to reperfuse the infarct vessel or a severe stenosis is present in the infarct vessel, a rescue PCI can be performed. A more conservative approach of elective PCI can be used to manage STEMI patients only when spontaneous or exercise-provoked ischemia occurs, whether or not they have received a previous course of fibrinolytic therapy.

SURGICAL REPERFUSION

Despite the extensive improvement in intraoperative preservation with cardioplegia and hypothermia and numerous surgical techniques it is not logistically possible to provide surgical reperfusion in a timely fashion. Therefore patients with STEMI who are candidates for reperfusion routinely receive either fibrinolysis or PCI. However, about 10 to 20 percent of STEMI patients are currently referred for coronary artery bypass grafting (CABG) for one of the following indications: persistent or recurrent chest pain despite fibrinolysis or PCI, high-risk coronary anatomy (e.g., left main stenosis) discovered at catheterization, or a complication of STEMI such as ventricular septal rupture or severe mitral regurgitation caused by papillary muscle dysfunction.[70,71]

RECURRENT CHEST PAIN

The most common cause of recrrent chest pain after AMI are coronary ischemia and pericarditis.

POSTINFARCTION ANGINA

Postinfarction angina is caused by recurring or worsening ischaemia after the initial acute necrosis.it is defined as chest pain that is frequently similar to the original discofort occurring at rest or with limited activity during hospitalization 24 hours or more after onset of the of AMI.This pain may or may not be associated with ST segment elevation or depression or with pseudonomalisation of inverted T waves on post n=myocardial ischaemia ECG. The incidence of AMI angina is almost twice as high after non Q myocardial infarction than Q wave myocardial infarction.Thrombolytic therapy also lead to a high incidence of post infarction angina,with a 12 – 15% incidence of reinfarction during te early experience with lytic therapy for reperfusion.

APPROACH TO POST INFARCTION ANGINA

If there is persistent pain lasing >30 minutes a reelevation of CK-MB and ST –T changes consider readministration of thrombolytic therapy (rt-PA).The other option is immediate coronary angiography and PTCA.

COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION

DYSARRHYTHMIAS

Bradycardia - Relatively common (30-40%) early in the course of acute myocardial infarction especially in inferior infarction or after reperfusion of right coronary artery because of activation of vagal afferents that ultimately result in enhanced parasympathetic tone .Atrpine in doses of 0.5 – 1mg is the drug of dose if hypotension tissue hypoperfusion coexists.[72]

AV BLOCK,VENTRICULAR ASYSTOLE

Atropine is useful for treatment of type 1 second degree AV block especially if complicating inferior wall MI and at times in third degree AV block of AV node in restoring AV conduction or for increasing functional response rate .For ventricular asystole atropine is used in doses of 1.0mg every 3-5 minutes during CPR upto a maximum of 2.5 mg if asystole persists.[73,74,48]

HEART BLOCK

A heart block in the stting Anterior MI reflects extensive infarction and concomitant destruction of the conducting system and is associated relatively high mortality. In contrast heart block with inferior myocardial infarction may primarily reflect ischemia of AV node rather than extensive tissue damage and so is associated with a better prognosis.[48,73]

VENTRICULAR FIBRILLATION

Ventricular fibrillation can occur in 3-5% acute myocardial infarction patients in the initial 4 hours. It is called primary VF. The mechanism is thought to be micro reentry in the infarct zone. Triggering factors include hypokalemia, hypomagnesemia, enhanced adrenergic tone ,acidosis, Increased intracellular calcium, increased free fatty acids and reperfusion induced production of free radicals. Incidence of VF is decreased by the use of beta blockers .Prompt defibrillation using unsynchronized shock starting with 200j is the treatment of choice.If unsuccessful give another shock immediately with 200-300 J.If again persists shock with energy level of 360J.[48,73]

VENTRICULAR TACHYCARDIA

Polymorphic VT causing hemodynamic collapse is treated with unsynchronized shock starting with 200 J. monomorphic VT with hypotension pulmonary edema or angina should be treated with a synchronized shock with an energy level starting at 100 J initially. Hemodynamically stable ventricular tachycardia is treated with intravenous lidocaine 1-1.5 mg/kg IV bolus with supplemental doses of 0.5 -0.75 mg /kg every 5 -10 minutes upto a maximum of 3 mg /kg if needed.This is followed by an onfusion of 2 – 4mg /min for 24 hours . Other dysrrhythmia that can

occur during Acute myocardial infarction are ventricular ectopics,atrial flutter and fibrillation, functional rhythm.[48,75,76]

ACCELERATED IDIOVENTRICULAR RHYTHM

Normally occur frequently during the first hours of acute myocardial infarction and occur after thrombolysis as a perfusion arrhythmia. Accelerated idioventricular rhythm should not be treated .When the rate exeed 120 mg /mt it should not be treated. When the rate exeed 120/mt it should be considered as an autonomic rhythm for which suppression with lidocaine should be considered.[48,75,76]

MECHANICAL COMPLICATIONS

Mechanical complications are cardiogenic shock papillary muscle dysfunction ,papillary muscle rupture ,ventricular septal rupture,cardiac rupture ,ventricular aneurysm formation and pseudoaneurysm.

CARDIOGENIC SHOCK

Cardiogenic shock may occur when 40% or more of left ventricle is infracted .It is the most common cause of in hospital death in acute myocardial infarctionpatients .mortality rate is around 80%.The incidence of cardiogenic shock has decreased from 15% in the early 1970s to

approximately 5-7% . This is attributed to use of thrombolytic therpy and better treatment of angina and ischemia.

Characteristics of cardiogenic shock are 1) Evidence of hypoperfusion : Cold. clammy skin, impaired mentation, oliguria. 2) Systolic blood pressure < 80-90mm Hg. 3) Left ventricular end diastolic pressure or pulmonary capillary wedge pressure ≥ 18 mmHg. 4) Evidence of primary cardiac abnormality. 4) Cardiac index ≤1.8/mt/ḿ.

MANAGEMENT OF CARDIOGENIC SHOCK

MAINTENANCE OF TISSUE PERFUSION

When systolic BP is more than 90 mm Hg intravenous dobutamine infusion is tried .When systolic pressure is below 70 – 90 mm Hg dopamine is the preferred agent so to bring the blood pressure to 90 – 100 mm Hg .If high doses of dopamine are necessary to maintaine adequate perfusion ,norepinephrine may be substituted for dopamine because norepinephrine has more alpha agonist effect and lesser chronotropic and ionotropic action of betareceptor stimulation. Early mechanical revascularization by PTCA or CABG improves survival .In the waiting period intra aortic balloon counter pulsation may be used to buy time .Thrombolytic therapy should be administered if facilities for percutaneous intervention procedures are available.

PAPILLARY MUSCLE RUPTURE

It occur in 1% of MI.Posteromedial papillary muscle is involved 6 – 12 times than that of anterolateral .Rupture occurs more often distally involving one or several of small heads of muscle .Usually manifests 2-7 days after infarction with the development of pulmonary edema.Mural valve replacement or repair is the treatment of choice.

PAPILLARY MUSCLE DYSFUNCTION

More common than rupture. Again poseromedial muscle is more often involved.Dysfunction may be transient during ischemia which can disappear with successful treatment.

VENTRICULAR SEPTAL RUPTURE

Incidence is 1-35 of acute myocardial infarction equally divided among anterior and inferior infarctio. It occur more often in first infarction and in the first week. Usually manifest by appearance of new harsh,holosystlic mrmur along the left sterna border and sudden clinical deterioration with hypotension and pulmonary congestion. Management is essentially surgical closure.

CARDIAC RUPTURE :

Free wall of the ventricle is the most common site of rupture . Generally occure within the first 2 weeks and may occur within 24 hours.It

occure more often in the first infarction, woman , elderly, and with systemic hypertension particularly if there is no associated left ventricular hypertrophy. It generally presents as sudden unanticipated death.

Other complications that may occur are pulmonary thromboembolism and systemic embolism.[77,78,79]

CONTINUING MANAGEMENT

Uncomplicated AMI patients can be transferred from CCU by 3rd day.

Materials and Methods

MATERIALS AND METHODS

PLACE OF STUDY

This study was conducted in the coronary care unit of Coimbatore medical college hospital, Coimbatore

PERIOD OF STUDY

From MARCH 2009 – OCTOBER 2010

DESIGN

Observational prospective cohort study of patients receiving streptokinase for acute myocardial infarction. A total of 83 patients were included in the study.

METHODOLOGY

Subject selection

1. Inclusion criteria

   a) Presence of typical chest pain suggestive of Acute myocardial infarction along with ECG evidence of acute myocardial infarction. Criteria for thrombolysis being 2mm or more ST elevation in two contiguous limb leads.

   b) Time window of 12 hrs from the onset of pain to the initiation of thrombolysis.

2. Exclusion criteria

   a) Late thrombolysis (more than 12 hrs from the onset of pain).

   b) Recurrent myocardial infarction.

   c) Presence of bundle branch block.

   d) Development of pericarditis.

DRUG THERAPY

- All patients received streptokinase 1.5 million units im 100 ml of normal saline over 60 minutes.

- Aspirin was given to all patients

- Use of hepain, Beta blockers , ACE inhibitors was according to CCU protocols which was in the accordance with ACC/AHA recommendations.

CRITERIA FOR SUCCESS OF THROMBOLYSIS

Success was defined by

1. Clinical complete subsidence of chest pain

2. Electrocardiographyically more than 50% ST resolution in a lead which showed maximum ST elevation initially. ST elevation is measured manually 80 ms after J point from isoelectric line .

Patients were analyzed for success of thrombolytic therapy at 90 minutes after initiation of thrombolytic therapy , applying the above mentioned criteria. Those who underwent successful thrombolysis were grouped into group A.

Those with failed thrombolysis grouped into group B

The following parameters were analyzed among them to know whether they influenced the outcome of thrombolysis.

(1) Age (2) Sex (3) Time of SK administration (4) Preinfarction angina (5) Alcohol intake (6) smoking status (7) Systemic hypertension (8) Diabetes mellitus (9) Location of MI (10) Time interval between the onset of pain and the initiation of thrombolytic therapy.

DEFINITIONS

Smoking : Patients are considered smokers if they were using tobacco for smoking in any form currently. Ex-smokers were defined as those who quitted smoking for more than 1 tear back from the date of admission.

Diabetes mellitus :- Patients were considered to be diabetic when

1. Currently on oral hypoglycemic drugs and /or insulin or
2. Fasting plasma glucose > 126 mg% or 2 hr post prandial plasma glucose >200mg% on more than 2 occasions.

Hypertension :- Patients were considered hypertensive when

1. They are already on the antihypertensive drugs
2. Medically documented Blood pressure elevation more than 140/90 mmHg, on two occasions in the past.

Preinfarction angina : It was defined as history of angina pain during the preceding 7 days of the acute event causing hospital admission.

Location of myocardial infarction : Inferior wall infarction :- In Patients with ST elevation ,with or without Q waves in leads ll, lll , aVF , are considered to have inferior wall infarction.

Anterior wall infarction : In Patients with ST elevation ,with or without Q waves in any two contiguous leads from V1 – V6 and L1 and aVL are considered to have anterior wall infarction.

FOLLOW UP

Patients were followed up until they were discharged from the hospital. ECHO evaluation was done whenever possible.

Statistical method : Univariate analysis was done by the chi-square test and multivariate analysis by logistic regression was done using SPSS windows computer software.

Observations and Results

OBSERVATIONS AND RESULTS

A total of 83 patients were studied. Their age ranged from 34 – 76 years (mean 55.03 yrs).68 of them were males (82%) and 15 females (18%) 20 of them were hypertensives (24%) .44 people were smokers (53%) and 29 (59%) consumed alcohol. 23 patients experienced preinfarction angina (28%) . 50 patients had anterior wall infarction (60%) and 33 patients (40%) had inferior infarction .

TABLE – 1

CLINICAL DETAILS OF STUDY POPULATION

ACCORDING TO THE OUTCOME OF THROMBOLYSIS

VRIABLE	SUCCESS (%)	FAILED (%)
NUMBER	44(53%)	39(47%)
MALES	36(53%)	32(47%)
FEMALES	8(53%)	7(47%)
HYPERTENSION	11(55%)	9(45%)
DIABETES	11(55%)	9(45%)
SMOKING	22(50%)	22(50%)
DRINKING	20(69%)	9(31%)
PREINFARCTION ANGINA	9(39%)	14(61%)
TIMEWINDOW		
0-4 HRS	21(64%)	12(31%)
4 -8 HRS	20(39%)	20(50%)
8-12 HRS	3(30%)	7(70%)
AGE GROUP		
<60 YRS	30(62%)	18(38%)
>60 YRS	14(40%)	21(60%)
ANTERIORWALL INFARCT	20(40%)	30(60%)
INFERIOR WALL INFARCT	24(72%)	9(28%)

TABLE-2

UNIVARIATE ANALYSIS FOR INFLUENCING FACTORS

S. No	Variables	Odds ratio	(X^2) Chi square	P Value	Comments
1	Age <60 years	2.50	4.11	0.04	Significant
2	Gender(female sex)		0.00	0.98	
3	Preinfarction angina	0.46	2.43	0.98	
4	Diabetes	1.11	0.04	0.83	
5	Hypertension		0.04	0.04	
6	Smoking		0.34	0.56	
7	Drinking	2.78	4.55	0.03	Significant
8	Infarct location (anterior)	0.25	8.55	0.004	Significant

TABLE – 3

LOGISTIC REGRESSION ANALYSIS

S. No	Variables	Odds(Ratio)	P Value	
1	Age <60 yrs	0.4036	0.09	
2	Dinking	3.16	0.06	
3	Location of MI	3.18	0.02	Significant
4	Smoking	0.34	0.08	

FIGURE 1
SUCCESS RATE WITH RESPECT TO INDIVIDUAL VARIABLES

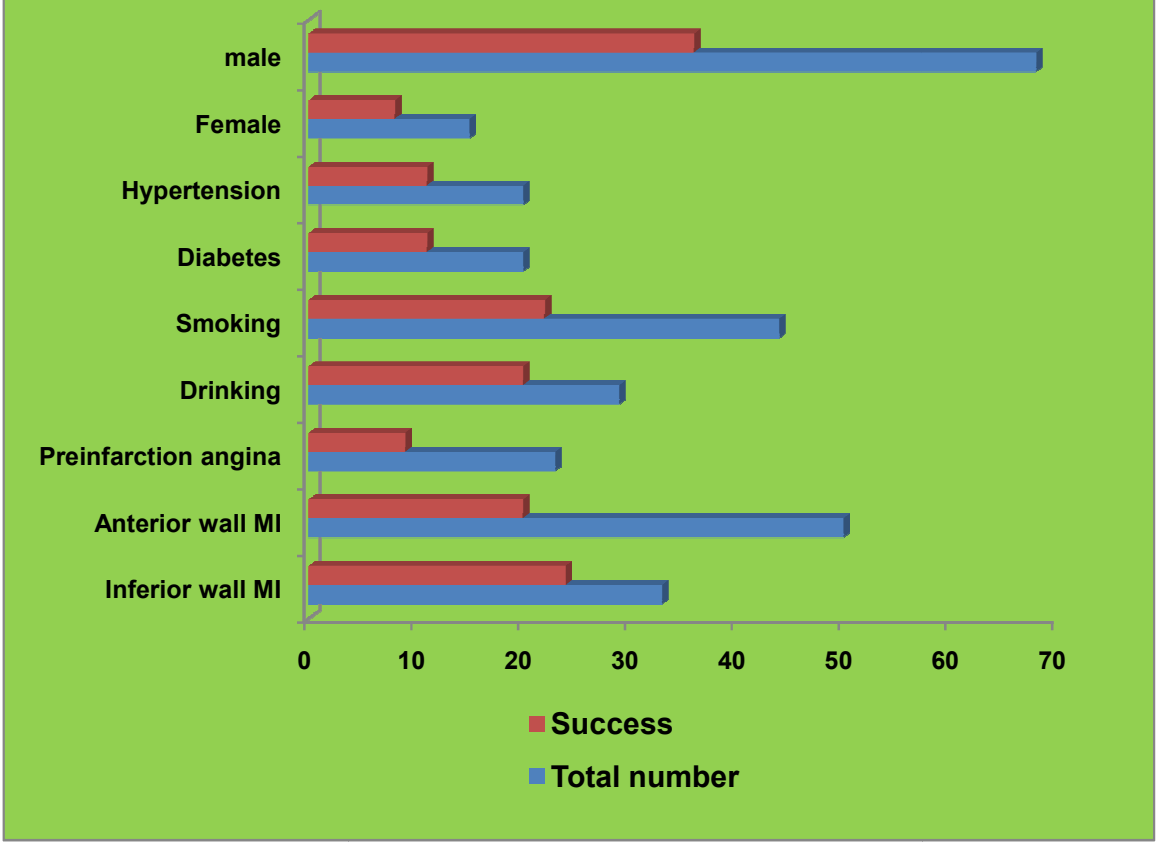


FIGURE -2 : OVERALL SUCCESS RATE OF THROMBOLYSIS

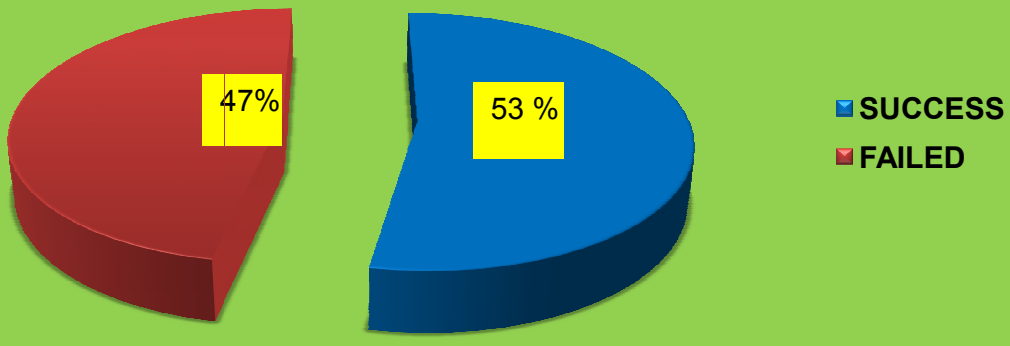


FIGURE 3
EFFECT OF TIME WINDOW ON THE SUCCESS RATE OF THROMBOLYSIS

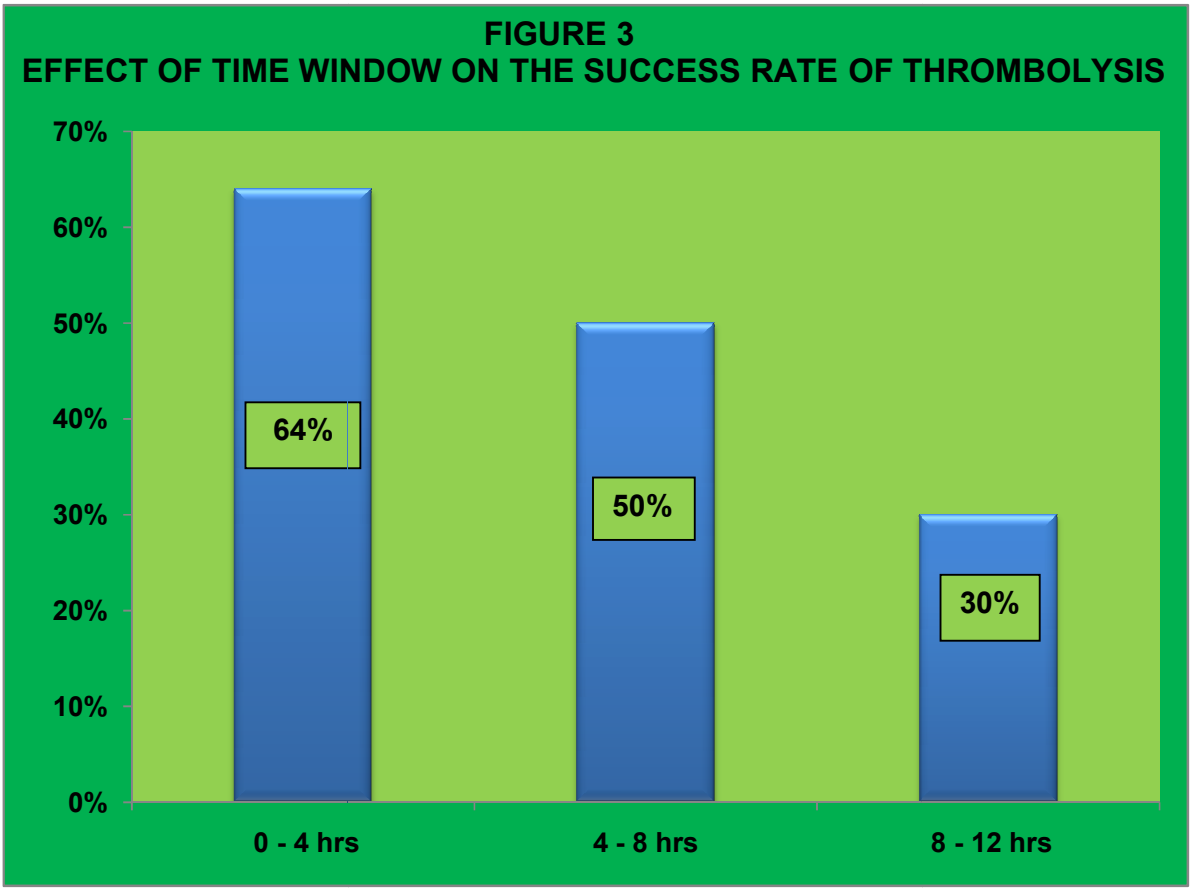


FIGURE 4
SEX DISTRIBUTION OF STUDY POPULATION

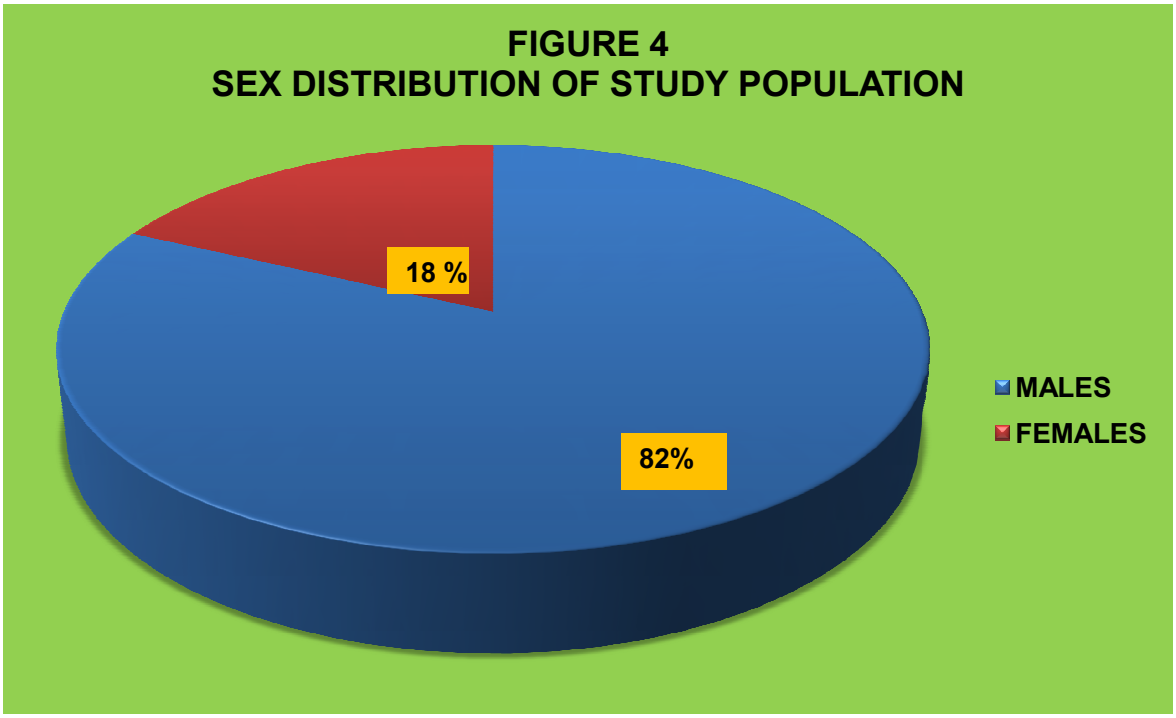


FIGURE 5
SUCCESS OF THROMBOLYSIS IN ANTERIOR WALL INFARCTIONS

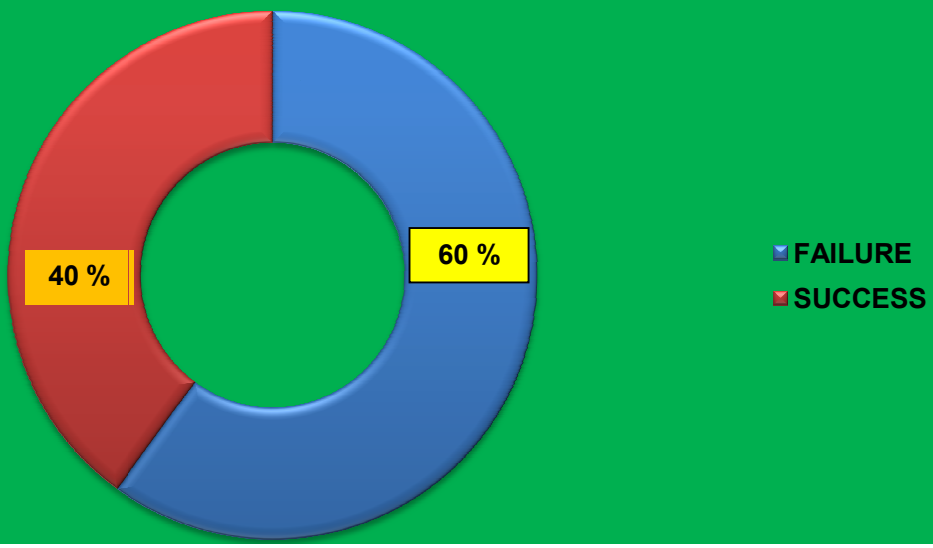
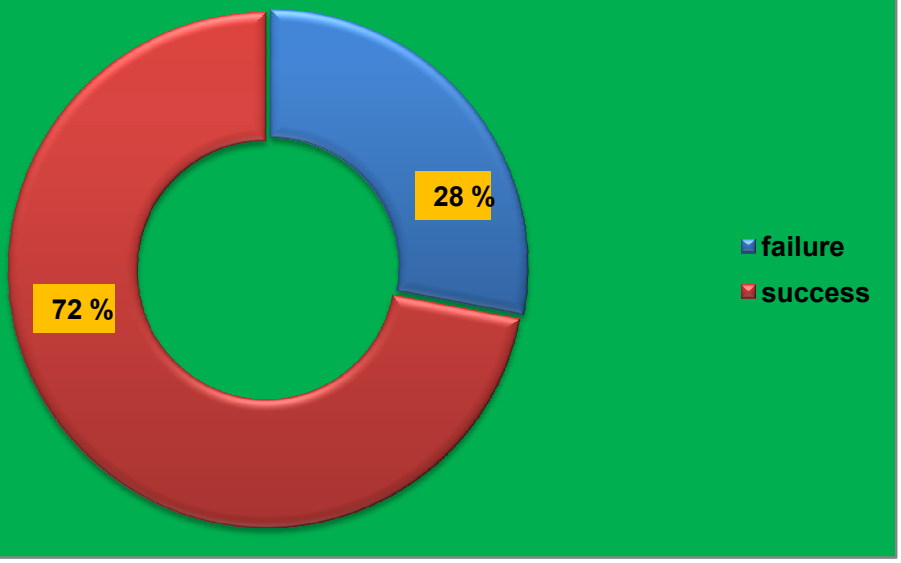


FIGURE - 6
SUCCESS OF THROMBOLYSIS IN INFERIOR WALL INFARCTION



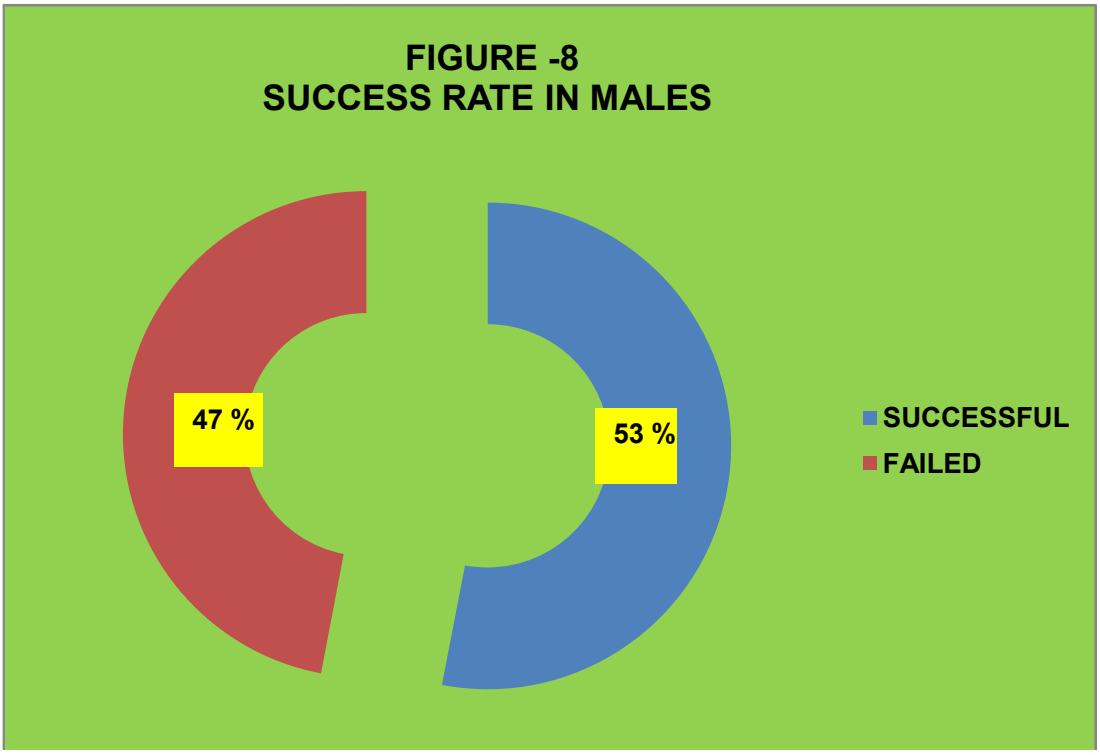


FIGURE -8
SUCCESS RATE IN MALES
47 %
53 %
SUCCESSFUL
FAILED

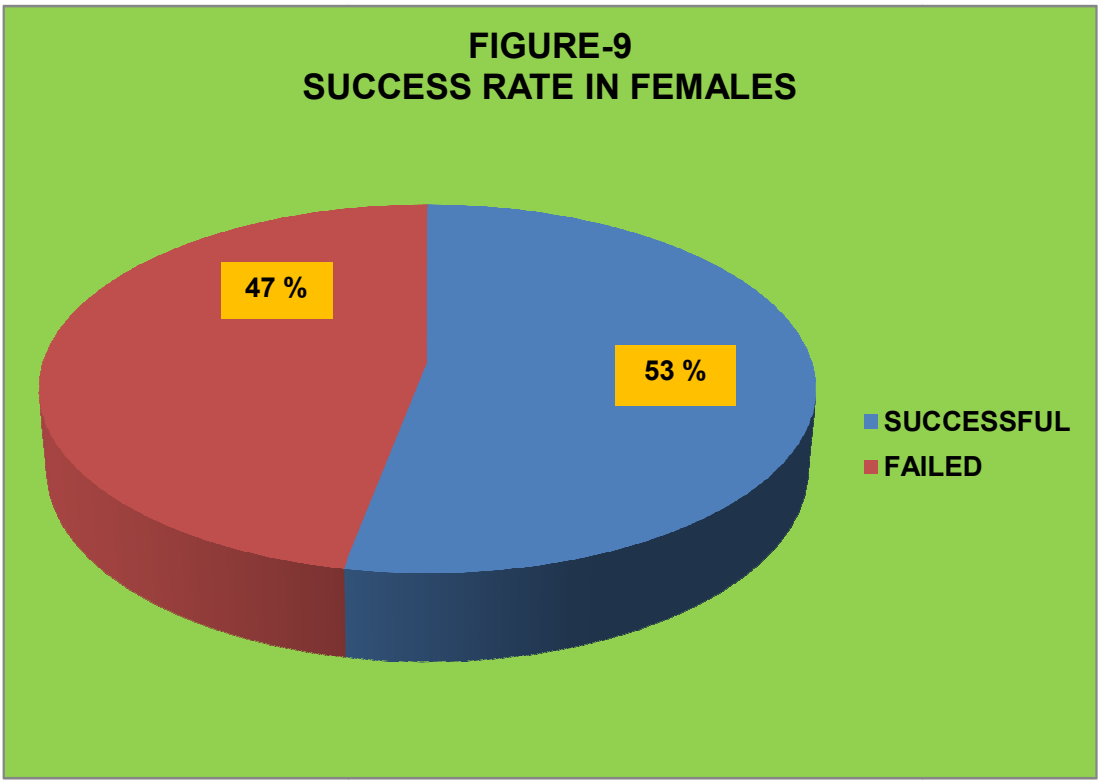


FIGURE-9
SUCCESS RATE IN FEMALES
47 %
53 %
SUCCESSFUL
FAILED

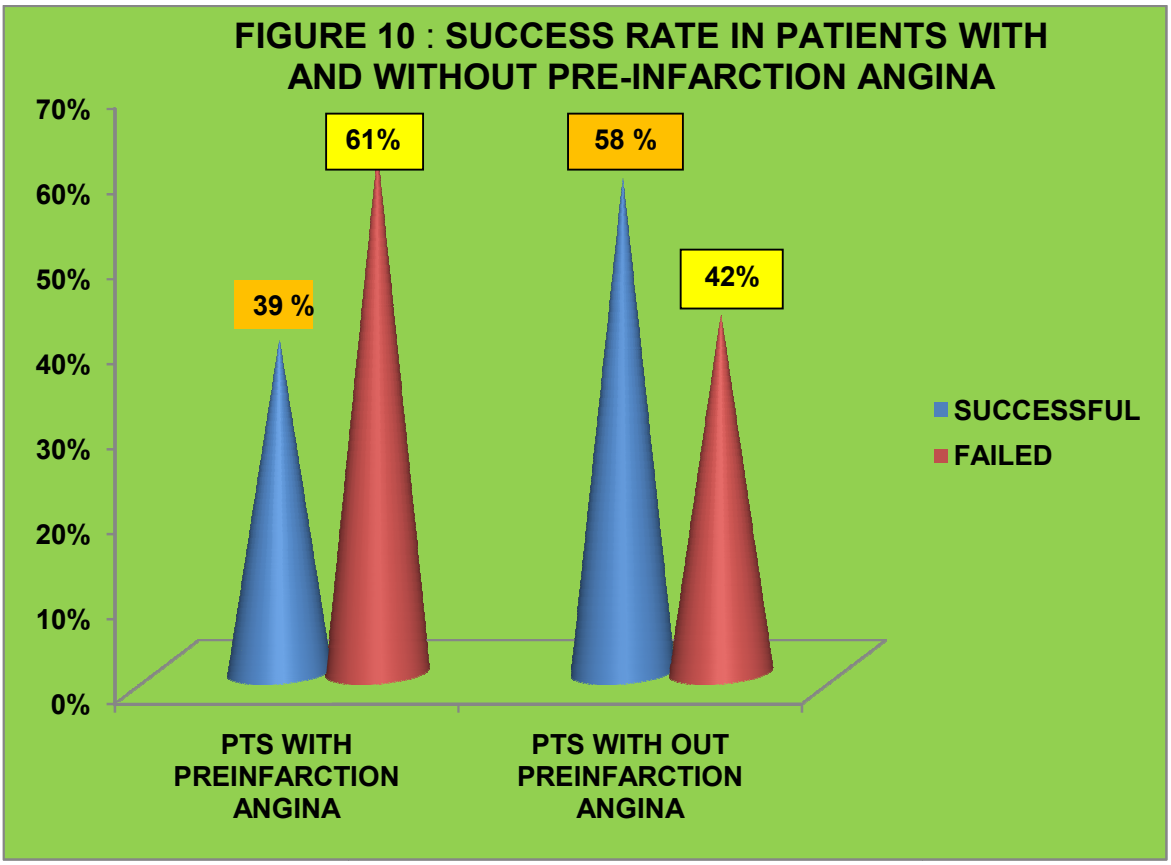


FIGURE 10 : SUCCESS RATE IN PATIENTS WITH AND WITHOUT PRE-INFARCTION ANGINA
70%
60%
50%
40%
30%
20%
10%
0%
61%
58 %
39 %
42%
SUCCESSFUL
FAILED
PTS WITH PREINFARCTION ANGINA
PTS WITH OUT PREINFARCTION ANGINA

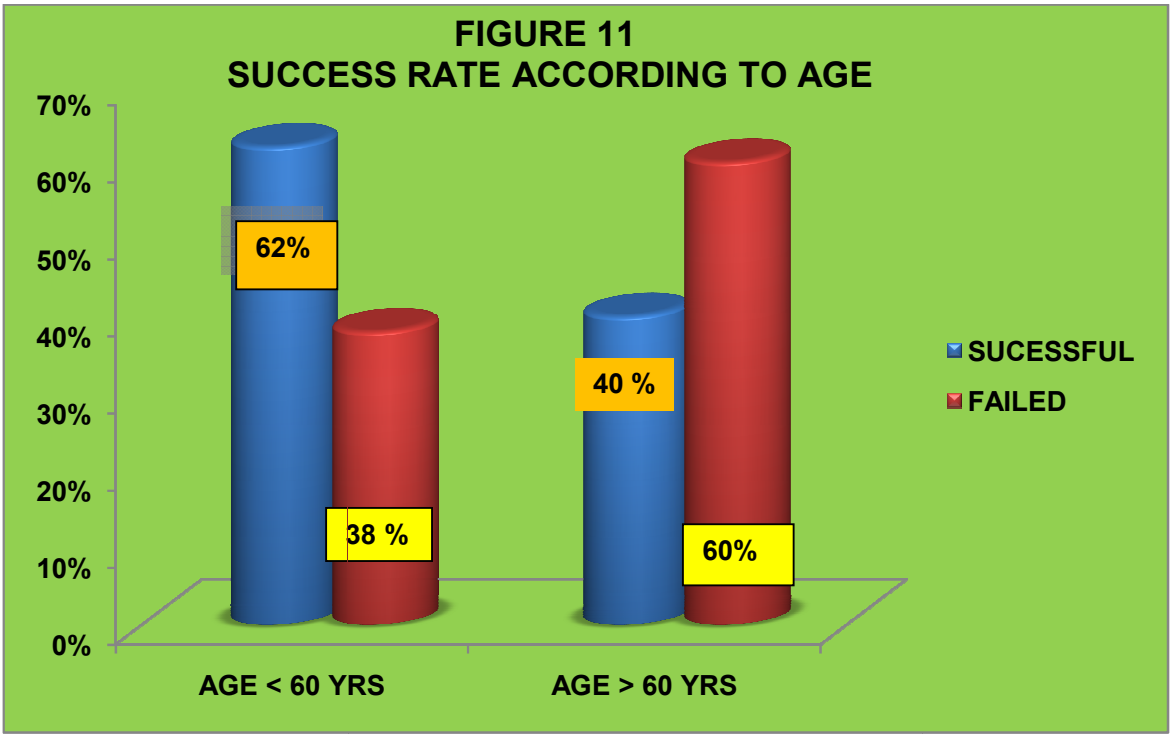


FIGURE 11
SUCCESS RATE ACCORDING TO AGE
70%
60%
50%
40%
30%
20%
10%
0%
62%
38 %
40 %
60%
SUCESSFUL
FAILED
AGE < 60 YRS
AGE > 60 YRS

Discussion

DISCUSSION

The major finding of this study is that the location of the infarct significantly affects the outcome of thrombolysis. Those with inferior wall myocardial infarction have a 3.18 times chance of undergoing successful thrombolysis compared to anterior wall myocardial infarction(p=0.02) .This is after adjustment for confounding variables like time window ,age ,smoking status, gender, diabetes and hypertension.

Similar observation was made by the Gibson ,Murphy and Braunwald et al(TIMIsubgroup). They found that TIMI grade lll flow rates were lower for left coronary and circumflex artery copared to right coronary artery after thrombolytic therapy.[80]

The reason for this differential response will be evident when we look into the physiology of coronary circulation in the left coronary arteries.

Blood flow in the right coronary artery is relatively independend of the phases of cardiac cycle being present in both systole and diastole. Where as flow in the left coronary artery is almost absent during systole and may even be reversed in conditions of heightened microvascular tone and left ventricular hypertrophy.[81]

The relatively thicker wall, the increased wall thickening during systolic contraction and higher intracavitory pressure of left ventricle may all produce higher intramyocardial pressure than that is observed in the thinner walled right ventricle which is also subjected to lower filling pressures.

More over the extent of necrosis in the anterior wall is more resulting in increased myocardial edeme copared to inferior infarctions. This may further decrease the reperfusion rates in anterior infarctions. Yet another mechanism may be, better drug delivery to the right coronary and prolonged contact of streptokinase with the thrombus ,resulting in more efficient fibrinolysis.

ALCOHOL AND THROMBOLYSIS

Alcohol consumption has influenced the outcome of the thrombolytic therapy in a favourable way. Univariate analysis revealed a success rate of 69% in the drinkers verses 44% in non drinkers.($p=0.03$,odds ratio=2.78). This advantage of drinkers persisted after logistic regression analysis to remove the confounding factors, even though statistically not significant . (odds ratio=3.16.$p=0.06$).

Alcohol is known to reduce coronary artery disease related mortality. In a meta analysis of all experimental studies that assessed the effects of moderate alcohol consumption on the concentrations of LDL cholesterol , apolipoprotein A1,fibrinogen, triglycerides and other biological markers

,Rimm,William,Fosher et al. [82] concluded that 30mg of alcohol /day would caus an estimated reduction of 24.7% in risk of coronary artery heart disease.

This better success rate observed in patients who consume alcohol may be easily explained by the effect of alcohol on hemostatic factors. In a study conducted on 631 apparently healthy male physicians the plasma levels of tPA antigen were 10.9, 9.7, 9.1, and 8.1ng/ml respectively in those who consumed alcohol daily, weekly, once a month and never. [83]

Studies have shown alcohol has an effect on platelets also. Alcohol reduces platelet aggregation in response to most agonists like thrombin, ADP, epinephrine and collagen.

By contrast in binge drinkers or in alcoholics after alcohol withdrawal response to aggregation especially that induced by thrombin is markedly increased. This rebound phenomenon may be explained ischemic strokes or sudden death known to occur after episodes of drunkenness.

Ehanol intake is also known to decrease blood fibrinogen level. Thus those who consume alcohol on a moderate basis are having better endogenous fibrinolytic response.

AGE OF THE PATIENT

Patients older than 60 years are found to have a lesser success rate in univariate analysis.(X2= 4.11,odds ratio = 2.5 ,P = 0.04). after adjustment

for other parameters in the logistic regression ,a statistically significant reduction in success rate is observed.

This shows that with respect to fibrinolysis elderly people do not behave diffently from younger. This is reflected in reduction in mortality rate among elderly after thrombolysis. In patients aged more than 75 yrs who were treated with streptokinase in GISSI-2 trial, there was a reduction of 4.2 fewer deaths per 100 patients than in controls.In ISIS- 2 there was 3.3 fewer deaths per 100 patients in those over 70 yrs of age who were treated. [84,88,89]

GENDER

No statistically significant difference was noticed based on the gender. Woodfield, Luderberg, topol et al .performed an angiographic study to find out the patency rate at 90 minutes in men verses women. At 90 minutes TIMI-3 flow rate was 39% in woman and 38% in men,which was not satistically significant. But 30 day mortality was 13.1 im women versus 4.8 in men($p=0.001$).[90,91,92,93] Thus even though females have a poor outcome after myocardial infarction, they donot behave differently to the thrombolytic therapy.

HYPERTENSION

Hypertensives did not show any difference in the success rate in thus study. High blood pressure often confers silent cardiovascular risk, and its prevalence is steadily increasing. Most epidemiological studies now

recognize the joint contributions of systolic and diastolic blood pressure to the development of cardiovascular risk, an issue that has markedly changed strategies for risk detection. The results of the TROPHY trial support treating prehypertensives and the feasibility of treatment. However, outcome trials demonstrating that the initiation of pharmacological therapy in prehypertensives indicated in the presence of other major comorbidities such as diabetes, renal dysfunction, or known vascular disease. Patients is superior to initiating treatment at the time of hypertension diagnosis are lacking. By contrast, pharmacological therapy is mandated for those with stage 1 hypertension (systolic blood pressure 140 to 159 mmHg or diastolic blood pressure 90 to 99 mmHg) or stage 2 hypertension (systolic blood pressure higher than 160 mmHg or diastolic blood pressure higher than 100 mmHg).[100]

DIABETES MELLITUS

In this study success rate of thrombolysis in diabetics is not found to be different from non diabetic population.

Gray, Yudkin et al. found a reduction in reperfusion rates in thrombolysed diabetic population. Diabetes is a prothrombotic state as reflected by the increased blood levels of fibrinogen, factor Vll and von willebrand factor. These changes are even more increased if diabetic people are happened to be smokers.[86,94]

Platelet function is also impaired in diabetics, They aggregate more readily to stimuli like ADP and collagen.Glycolisation of membrane proteins due to chronic exposure to high blood sugar levels change in the fluidity of platelet membrane brought out by high concentration of cholesterol and triglycerides are the proposed mechanisms for these abnormalities. On the other hand patients with type ll diabetes have profound suppression of fibrinolysis. Plasminogen activator inhibitor –l levels are high in type ll diabetic people which is responsible for this effect. Nevertheless thrombolytic therapy should be administered to diabetics with acute myocardial infarction, because for 100 diabetic patients treated with thrombolytic therapy four lives are saved.

PREINFARCTION ANGINA

Andreoti Vincenzo et al had demonstrated by angiographic method that those Acute myocardial patients who experienced preinfarction angina with in seven days preceeding the acute event had a more rapid thrombolysis. Patency rates were higher at 35 minutes but at 90 minutes both were same.[101]

In this study success rate was same at 90 minutes in both groups. This is because ECG monitoring was not continuous in this study. Continuous ST segment monitoring may be needed to demonstrate the early achievement of patency in preinfarction angina patients.[95,99]

SMOKING

Outcome of thrombolysis is not affected by the smoking. In this study there is stastically insignificant trent towards a bad outcome.

Gines Topol et al reported similar patency rates in smokers and non smokers at 90 minutes (73% verses 74%). Smokers tended to have reduced inhospital mortality compared to nonsmokers. but this was due to the favorable baseline clinical and angiographic variables in smokers. Smokers tended to be younger and thrombosis of less critical atherosclerotic plaque was the culprit lesion inthem. Smoking increases blood hematocrit ,fibrinogen levels and platelet levels contributing to the hypercoagulable state promoting coronary thrombosis. Smokers are also found to have lesser fibrinlytic activity than nonsmokers.[95,96,97,98]

PAIN TO STREPTOKINASE INTRAVAL(TIME WINDOW)

This is the most powerful predictor of success rate. In this study also it is evident. Success rate was 64% in those patients thrombolysed within 4 hours from the onset of symptoms. The success rate decreased to 55% when they were thrombolysed after 4 hours but within 8 hours of onset of chest pain. Success rate came down to 33% when streptokinase was administered after 8 hours but within 12 hours.[85,87]

Conclusion

CONCLUSION

1. In this study the overall success rate of Thrombolysis was 53 %.
2. The outcome was worse in those who aged more than 60 years. But it was not statistically significant.
3. Gender was not found to influence the success rate of thrombolysis.
4. Pre infarction angina had no effect on the success rate of thrombolysis.
5. Better success rate has been seen in those consuming alcohol which was not statistically significant.
6. Smokers had a lesser success rate than non smokers but it did not reach any statistical significance.
7. Hypertensives did not show any difference with non hypertensives in the success rate.
8. Diabetics did not differ from non diabetics with respect to the success rate of thrombolysis.
9. Inferior wall myocardial infarction had a better success rate than anterior wall myocardial infarctions and was statistically significant.
10. Those who are having short window period had a better success rate after thrombolysis. Shorter the window period higher the success rate.

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Appendix

Abbreviations

LIST OF ABBREVIATIONS USED IN THE PROFORMA AND IN THE DISSERTATION

AMI	:	Acute Myocardial Infarction
PAI -1	:	Plasminogen Activator Inhibitor – 1
PDGF	:	Platelet Derived Growth Factor
VVW	:	Von Willebrand factor
APSAC	:	Anisollated Plasminogen Streptokinase Activator Complex
LBBB	:	Left Bundle Branch Block
RBBB	:	Right Bunle Branch Block
RCA	:	Right Coronary Artery
LCA	:	Left Coronary Artery
LCX	:	Left Circumflex Artery
LAD	:	Left Anterior Descending
PTCA	:	Percutaneous Transluminal Coronary Angioplasty
SK	:	Steptokinase
rtPA	:	Recombinant tissue plasminogen Activator
LV	:	Left Ventricle
RV	:	Right Ventricle
VF	:	Ventricular Fibrillation
VT	:	Ventricular tachycardia
CABG	:	Coronary Artery Bypass Graft
ECG	:	Electro cardio graph

Proforma

PROFORMA

NAME : AGE : SEX :

ADDRESS : OCCUPATION :

HISTORY

CHEST PAIN : DURATION : LOCATION :

ASSOCIATED SYMPTOMS :

SWEATING RADIATION OF PAIN

PALPITAION BREATHLESSNESS

PAST HISTORY OF

SYSTEMIC HYPERTENSION (DURATION) :

DIABETIC MELLITUS (DURATION) :

CORONARY ARTERY DISEASE(DURATION) :

SMOKING :

ALCOHOL CONSUMPTION :

GENERAL EXAMINATION :

PALLOR/JAUNDICE/CYNOSIS/CLUBBING/PEDAL EDEMA PULSE :

BLOOD PRESSURE (AT THE TIME OF ADMISSION) :

RESPIRATORY RATE :

TEMPERATURE :

SYSTEM EXAMINATION

CARDIOVASCULAR SYTEM

S1 ,S2, S3 ,MURMUR , ADDED SOUNDS :

RESPIRATORY SYSTEM

BREATH SOUNDS , ADVENTITIOUS SOUNDS :

ABDOMINAL EXAMINATION

ORGANOMEGALY, FREE FLUID :

NERVOUS SYSTEM

ANY FOCAL NEUROLOGICAL DEFICITS :

ECG:

AT THE TIME OF ADMISSION :

PRESENCE OF BUNDLE BRANCH BLOCKS , ARRHYTHMIAS :

LOCATION OF MYOCARDIAL INFARCTION :

AFTER THROMBOLYSIS :

TREATMENT

TIME INTRAVAL BETWEEN THE ONSET OF PAIN AND THE INITIATION OF THROMBOLYTIC THERAPY:

EFFECT OF THROBOLYSIS:

CLINICALLY COMPLETE SUBSIDENCE OF CHEST PAIN :

ECG - MORE THAN 50% ST-RESOLUTION (SUCCESSFUL THROMBOLYSIS)

Consent Form

DEPARTMENT OF GENERAL MEDICINE ,

COIMBATORE MEDICAL COLLEGE HOSPITAL.

STUDY ON FACTORS INFLUENCING OUTCOME OF THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION

Informed consent form for prospective participants

Principal Investigator : Dr Pratheesh P. P, Junior Resident.

Research Guide : Prof. Dr Raveendran .MD,Chief, Medical Unit – IV.

Organization : Department of Medicine, Coimbatore Medical College Hospital.

This informed consent form has two parts

PART – I INFORMATION SHEET(to share the information about the research with you)

PART – II CERTIFICATE OF CONSENT (for signatures if you agree to take part)

(You will be given a copy of the full informed consent form.)

PART – I INFORMATION SHEET

I , Dr Pratheesh P.P, Junior resident in Dept of Medicine invites you to join as participant in my research on thrombolysis in acute myocardial infarction . I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.

Thrombolysis in acute myocardial infarction is a life saving procedure. By lysing the thrombus and successful reperfusion , further injury to the myocardium can be prevented. We are doing this research to predict the outcome of thrombolysis and thereby focus our prevention and treatment efforts in a better way.

In this study you will have to answer questions regarding your illness, undergo a physical examination , give urine and blood for tests, undergo a radiological exam of chest and an electrocardiogram.

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will

continue and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

You will have to give details regarding your age, duration of disease, family history of the disease, any symptoms you are having at present, your past medical problems, surgeries and current medications. A doctor will examine you to look for any problems. Your height and weight will be recorded. All the data will be recorded in a proforma. Ten ml of blood will be drawn for doing various laboratory tests to know about the status of your disease. Any excess sample will be destroyed immediately after the laboratory tests are completed. Taking the blood sample will produce some pain and there may be slight redness at the site of puncture for a day or two. Also you will have to provide 3 ml or urine for tests to detect protein. You will be subjected to a radiological exam of the chest and an electrocardiogram(ECG) will be recorded all of which are painless procedures.

On the first day you will be asked about your problems, a doctor will check you up and an ECG will be taken. You will also have to give the blood and urine samples. A chest x-ray will also be taken

In total you will have to visit twice or thrice for the research purpose. By participating in this research it is possible that you may experience some discomfort as each of your visits will take longer than your usual bi-weekly follow up visits and will involve needle pricks to give blood samples.

If you participate in this research you will be having a thorough check up, which may reveal some unidentified problems in you. We will promptly start the treatment for them. Also by participating you are providing valuable data that will help doctors understand this disease better and ultimately serve the patients in a better way.

We will not be providing any money for participating in this research, you may incur more expense since you will have to visit the hospital more frequently.

It is possible that if others in the community are aware that you are participating in this research, they may ask you questions. We will not be sharing the identity of those participating in the research with anyone. The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will not be identified by your name but by a number. Only the researchers will know what your number is and they will lock that information up with a lock and key. It will not be shared with or given to anyone except my research guide.

The knowledge that we get from doing this research will be shared with you before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. After these meetings, we will publish the results in order that other interested people may learn from our research

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact

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Coimbatore Medical College Hospital,
Coimbatore- 18.

This proposal has been reviewed and approved by the Ethics Committee of Coimbatore Medical College Hospital which is a committee whose task it is to make sure that research participants are protected from harm.

PART – II CERTIFICATE OF CONSENT

I have been invited to participate in research on diabetes. I understand that it will involve answering a detailed questionnaire, undergoing a thorough physical exam, giving blood and urine samples and two or three follow-up visits. I have been informed that the risks are minimal and may include only slight pain and redness at sight of needle prick. I am aware that there may be no benefit to me personally and that I will not be compensated monetarily. I have been provided with the name of a researcher who can be easily contacted using the number and address I was given for that person.

I have read the foregoing information or it has been read to me. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research and understand that I have the right to withdraw from the research at anytime without in anyway affecting my medical care.

Name of the participant: _____

Signature of the participant: _____

Date: _____

(Day/Month/Year)

If illiterate

A literate witness must sign (if possible , this person should be selected by the participant and must have no connection to the research team)

I have witnessed the accurate reading of the consent form to the potential participant , translated to his mother tongue, and the individual has had opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness : _____ AND Thumb print of participant

Signature of witness : _____

Date : _____

(Day/Month/Year)

I have accurately read or witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of the researcher : _____

Signature of the researcher : _____

Date : _____

(Day/Month/Year)

Master Chart

Sl.no	IP.no	Age	Sex	Hyper-tension	Diabetes	Smoking	Alcohol	Preinfarction Angina	Location of MI	Window period (hrs)	Successful thrombolysis
1	11378	48	MALE	NO	NO	YES	YES	NO	INFERIOR	3	YES
2	11962	49	MALE	YES	NO	YES	YES	YES	ANTERIOR	6	NO
3	13877	46	MALE	NO	NO	NO	NO	NO	ANTERIOR	4	NO
4	13374	54	FEMALE	YES	NO	NO	NO	YES	ANTERIOR	7	YES
5	15632	63	MALE	NO	NO	YES	NO	NO	INFERIOR	10	NO
6	15765	58	FEMALE	NO	NO	NO	NO	NO	INFERIOR	7	NO
7	17945	48	MALE	NO	YES	YES	YES	NO	INFERIOR	4	YES
8	19786	52	MALE	YES	NO	NO	YES	NO	INFERIOR	4	YES
9	24367	66	FEMALE	NO	NO	NO	NO	YES	ANTERIOR	7	YES
10	27654	67	MALE	YES	YES	NO	NO	YES	ANTERIOR	4	NO
11	29567	68	MALE	NO	YES	YES	NO	NO	INFERIOR	3	YES
12	32786	43	MALE	NO	NO	YES	YES	NO	ANTERIOR	7	YES
13	26987	54	MALE	NO	YES	NO	YES	YES	ANTERIOR	1O	NO
14	29879	41	MALE	NO	NO	YES	YES	NO	INFERIOR	8	YES
15	23678	59	FEMALE	YES	YES	NO	NO	NO	ANTERIOR	4	YES
16	27652	62	MALE	NO	NO	NO	NO	NO	INFERIOR	7	NO
17	29806	34	MALE	NO	NO	YES	YES	NO	ANTERIOR	3	YES
18	31432	51	MALE	NO	NO	NO	NO	NO	ANTERIOR	4	NO
19	34786	52	MALE	NO	NO	YES	YES	NO	ANTERIOR	6	YES
20	36478	70	FEMALE	NO	NO	NO	NO	NO	INFERIOR	10	YES
21	38765	68	MALE	YES	NO	YES	YES	YES	ANTERIOR	3	NO
22	39765	49	MALE	NO	NO	YES	NO	NO	ANTERIOR	6	NO
23	41435	56	FEMALE	NO	YES	NO	NO	NO	INFERIOR	7	NO
24	42598	49	MALE	YES	NO	YES	YES	YES	INFERIOR	4	YES
25	45698	62	MALE	NO	NO	NO	NO	NO	ANTERIOR	8	NO
26	47896	76	MALE	NO	YES	YES	NO	NO	INFERIOR	5	YES

27	48089	48	MALE	NO	NO	YES	NO	NO	ANTERIOR	11	NO
28	49780	54	MALE	NO	NO	YES	YES	NO	ANTERIOR	8	NO
29	50098	53	MALE	NO	NO	YES	YES	NO	INFERIOR	9	YES
30	50978	66	FEMALE	NO	NO	NO	NO	NO	ANTERIOR	8	NO
31	52356	56	MALE	NO	NO	NO	NO	NO	INFERIOR	4	YES
32	56409	58	MALE	YES	YES	YES	NO	YES	ANTERIOR	4	NO
33	56998	64	MALE	NO	NO	YES	YES	NO	INFERIOR	5	YES
34	57664	50	MALE	YES	NO	NO	NO	YES	ANTERIOR	6	YES
35	57699	61	MALE	NO	NO	YES	YES	NO	ANTERIOR	10	NO
36	58997	47	MALE	NO	NO	NO	NO	NO	ANTERIOR	8	NO
37	59076	55	FEMALE	NO	NO	NO	NO	NO	ANTERIOR	4	YES
38	60885	61	MALE	NO	NO	YES	NO	NO	INFERIOR	6	NO
39	60994	42	MALE	YES	NO	NO	NO	YES	ANTERIOR	4	NO
40	61445	51	MALE	NO	NO	YES	YES	NO	INFERIOR	2	YES
41	65890	63	MALE	NO	NO	YES	YES	NO	ANTERIOR	8	NO
42	62347	45	MALE	NO	YES	YES	NO	NO	INFERIOR	5	YES
43	67497	65	FEMALE	NO	YES	NO	NO	NO	ANTERIOR	10	NO
44	68795	67	MALE	NO	NO	YES	NO	NO	ANTERIOR	7	YES
45	68907	51	MALE	YES	NO	YES	YES	YES	INFERIOR	4	YES
46	69876	65	FEMALE	NO	YES	NO	NO	NO	INFERIOR	6	YES
47	69976	55	MALE	NO	NO	YES	YES	NO	ANTERIOR	4	NO
48	70986	72	MALE	NO	NO	NO	NO	YES	ANTERIOR	4	NO
49	71456	55	MALE	NO	NO	YES	NO	NO	ANTERIOR	6	YES
50	71987	68	MALE	YES	YES	NO	NO	YES	INFERIOR	12	NO
51	72997	57	MALE	NO	NO	YES	NO	NO	ANTERIOR	8	NO
52	67859	58	MALE	YES	YES	NO	YES	YES	INFERIOR	3	YES
53	98065	64	FEMALE	NO	NO	NO	NO	YES	INFERIOR	8	NO
54	89750	53	MALE	NO	NO	YES	NO	NO	ANTERIOR	4	NO
55	89765	54	FEMALE	NO	NO	NO	NO	NO	ANTERIOR	9	YES

56	89706	68	MALE	YES	NO	YES	NO	NO	INFERIOR	5	YES
57	76504	47	MALE	NO	NO	YES	YES	NO	ANTERIOR	6	YES
58	79806	51	MALE	NO	NO	NO	NO	NO	ANTERIOR	8	NO
59	78640	67	MALE	YES	NO	NO	NO	YES	ANTERIOR	6	YES
60	74650	44	MALE	NO	NO	NO	NO	NO	INFERIOR	4	YES
61	67548	66	MALE	NO	YES	YES	NO	YES	ANTERIOR	8	NO
62	67858	66	MALE	NO	NO	YES	YES	NO	ANTERIOR	8	NO
63	87659	49	MALE	NO	NO	YES	NO	NO	ANTERIOR	3	YES
64	98765	64	FEMALE	YES	NO	NO	NO	YES	INFERIOR	4	NO
65	67975	62	MALE	NO	YES	NO	YES	NO	INFERIOR	6	YES
66	94532	46	MALE	NO	NO	NO	NO	YES	ANTERIOR	5	YES
67	99567	67	MALE	NO	NO	YES	NO	NO	ANTERIOR	10	NO
68	89765	50	MALE	NO	NO	YES	NO	NO	ANTERIOR	8	NO
69	87659	64	MALE	NO	YES	YES	YES	NO	INFERIOR	3	YES
70	91342	57	MALE	YES	NO	NO	NO	YES	ANTERIOR	6	YES
71	96045	61	MALE	NO	YES	YES	NO	NO	ANTERIOR	4	NO
72	98564	60	MALE	NO	NO	NO	NO	NO	ANTERIOR	8	NO
73	90675	50	MALE	NO	NO	YES	YES	NO	INFERIOR	4	YES
74	95643	68	MALE	YES	NO	NO	NO	YES	ANTERIOR	8	NO
75	98748	48	MALE	NO	NO	NO	NO	NO	INFERIOR	4	YES
76	98750	67	MALE	NO	NO	YES	YES	NO	ANTERIOR	3	YES
	97604	56	FEMALE	YES	YES	NO	NO	YES	INFERIOR	8	NO
78	98765	38	MALE	NO	NO	NO	YES	NO	ANTERIOR	4	YES
79	90436	61	FEMALE	YES	YES	NO	NO	YES	ANTERIOR	6	YES
80	90862	67	MALE	NO	NO	YES	YES	NO	ANTERIOR	4	NO
81	97651	56	MALE	NO	NO	YES	YES	NO	INFERIOR	4	YES
82	98067	66	MALE	NO	NO	YES	NO	NO	INFERIOR	8	YES
83	99453	53	MALE	NO	YES	YES	NO	NO	ANTERIOR	4	YES